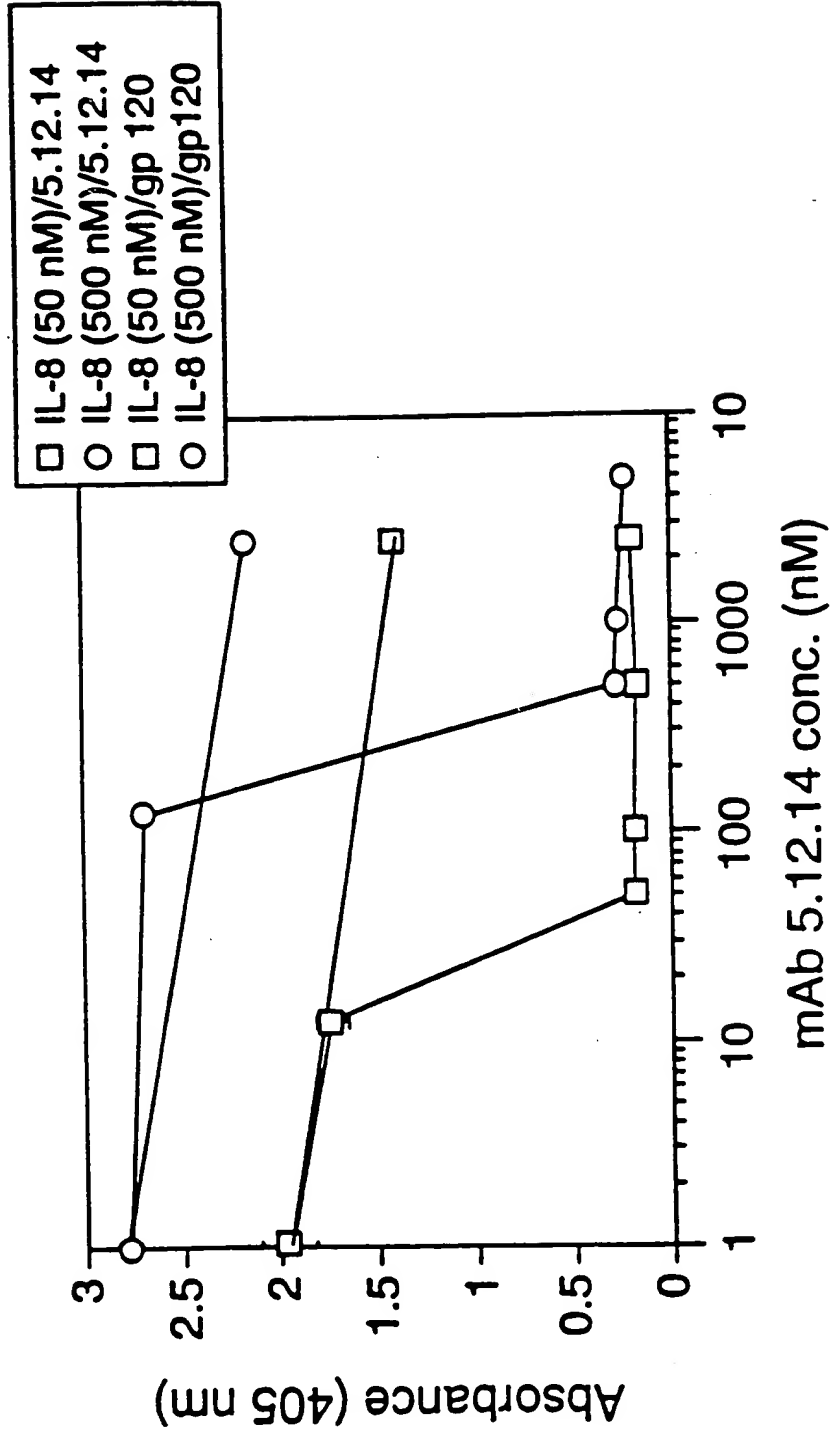


FIG. 1



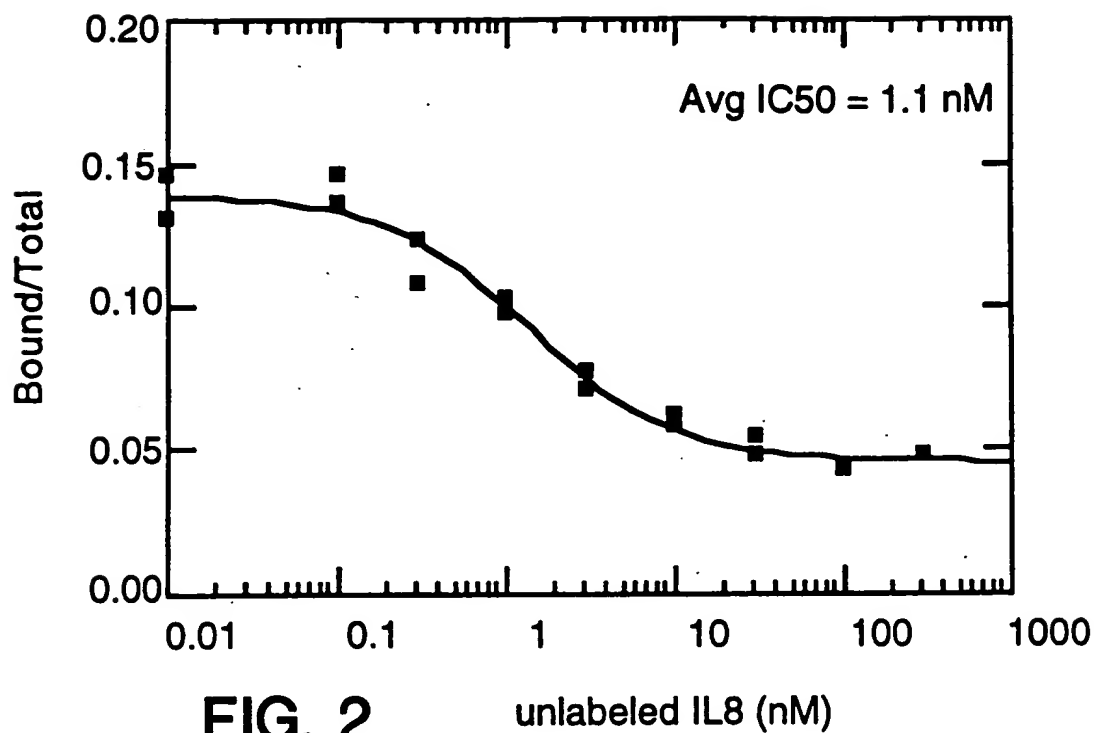


FIG. 2

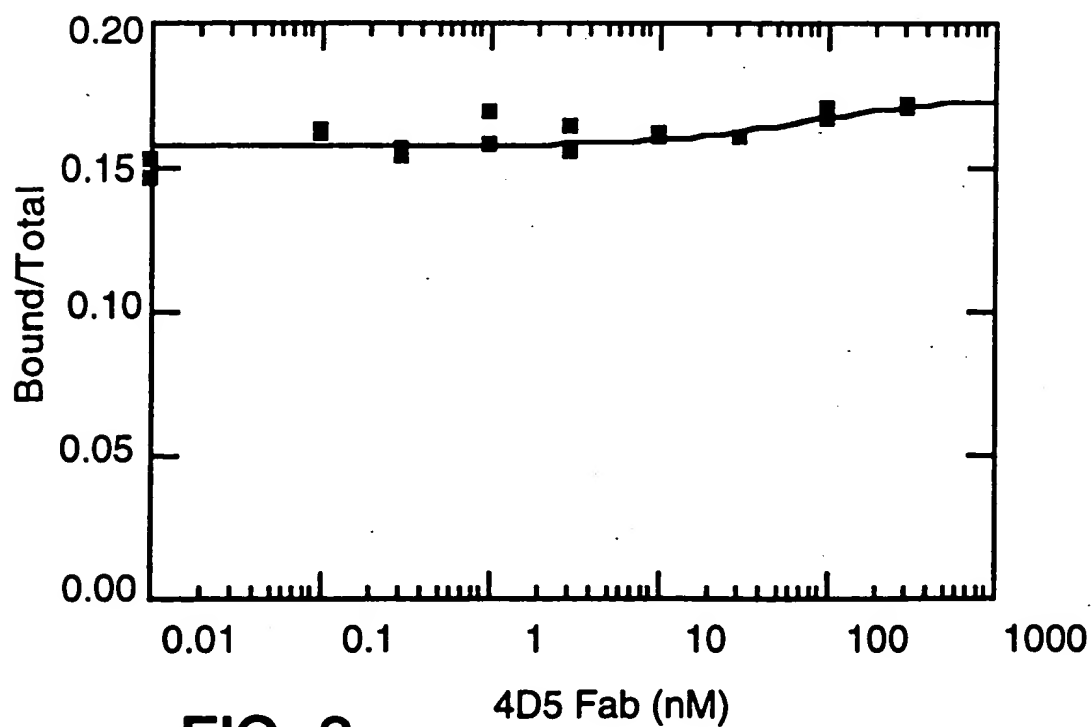
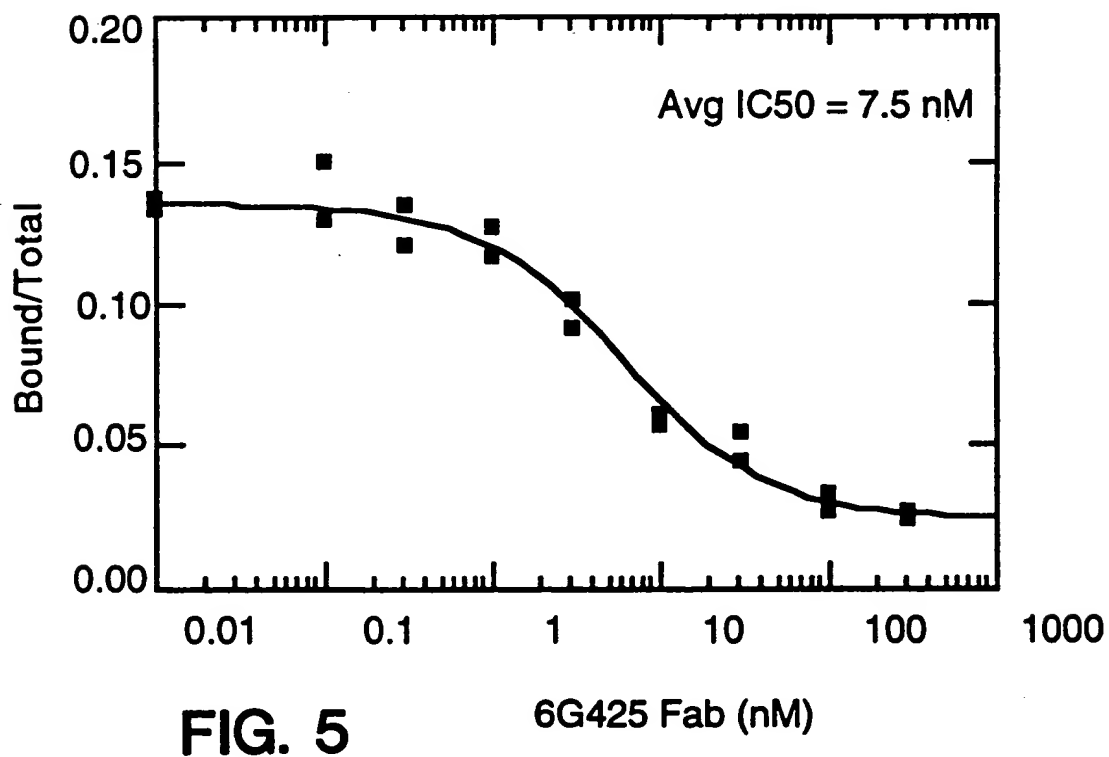
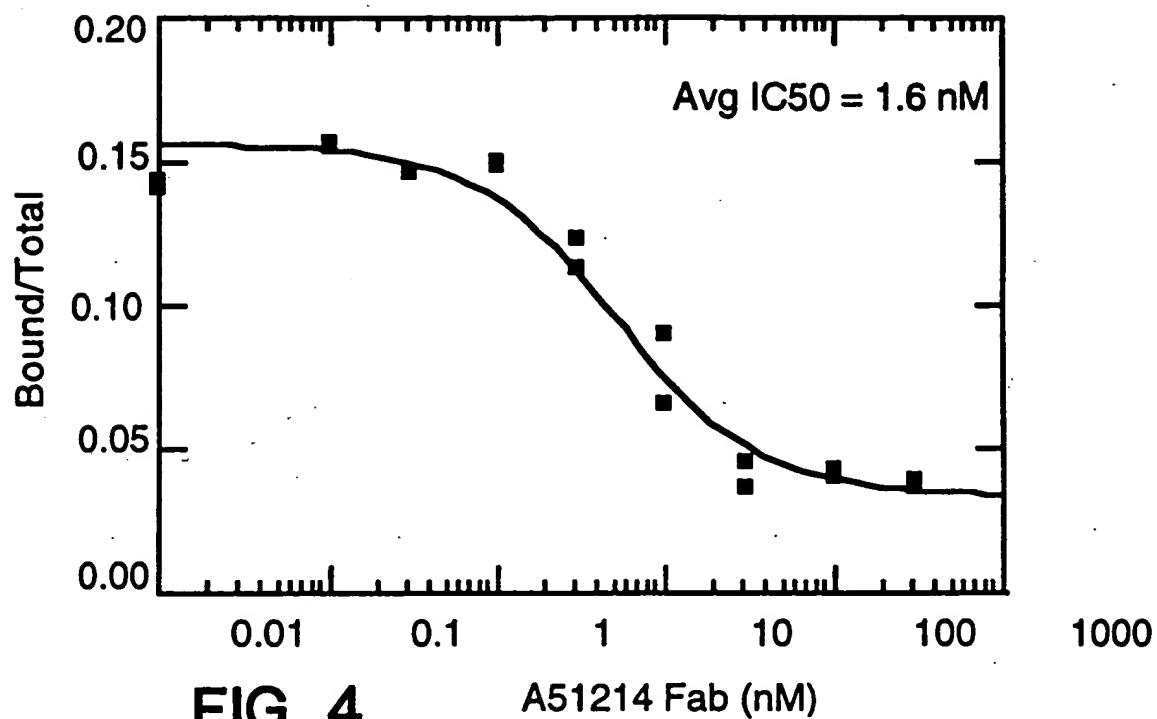


FIG. 3



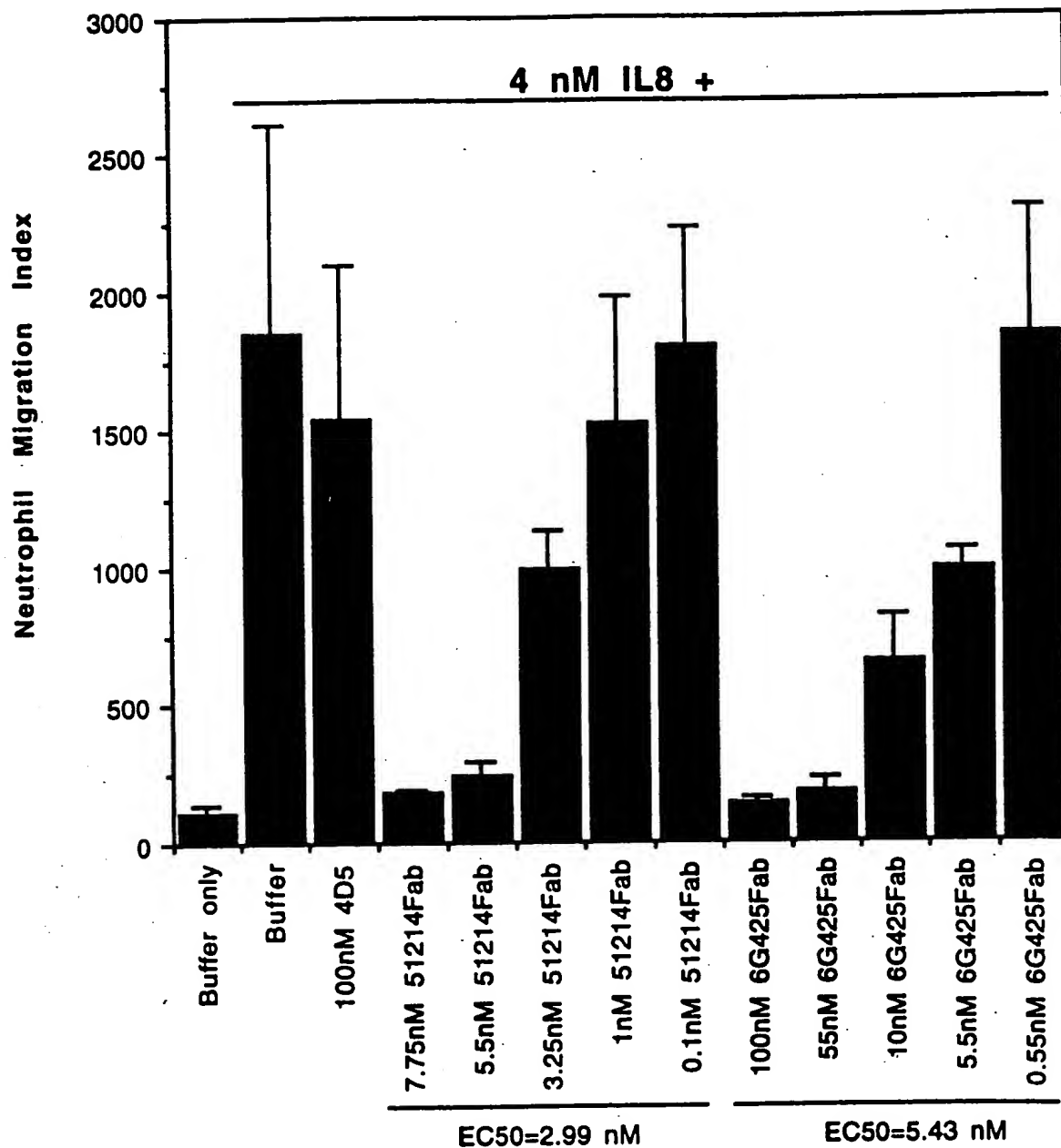


FIG. 6

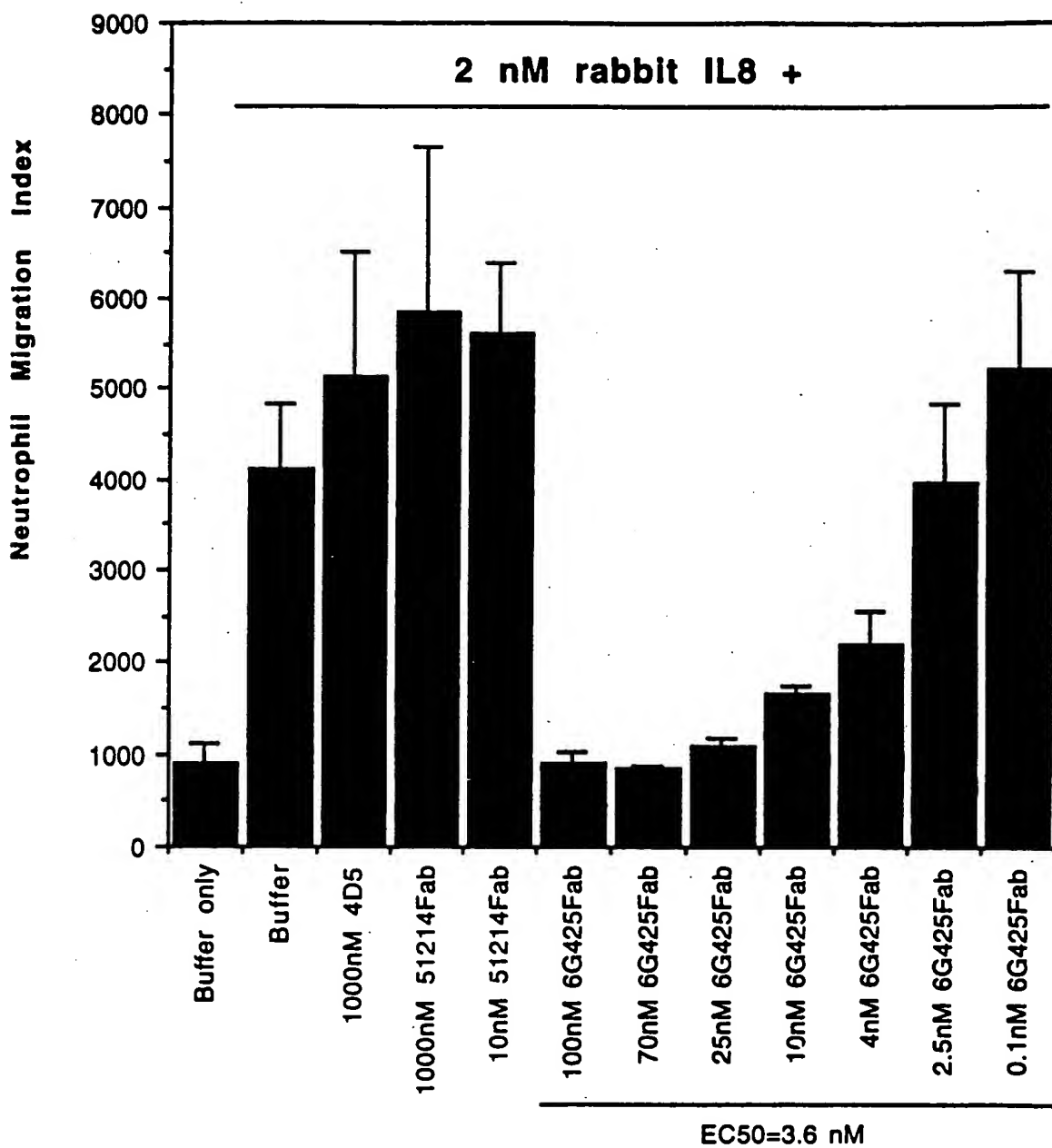


FIG. 7

FIG. 8

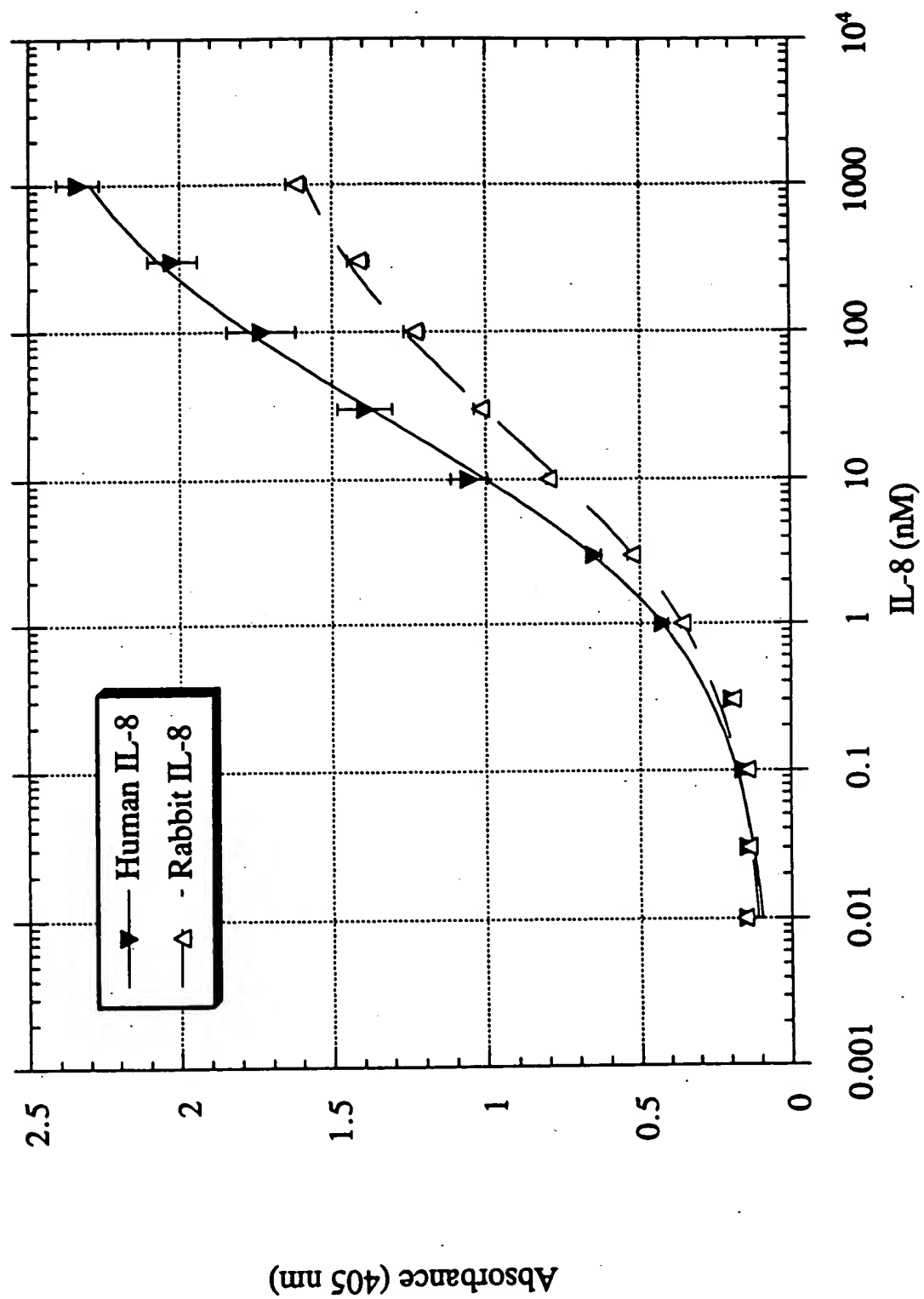


FIG. 9

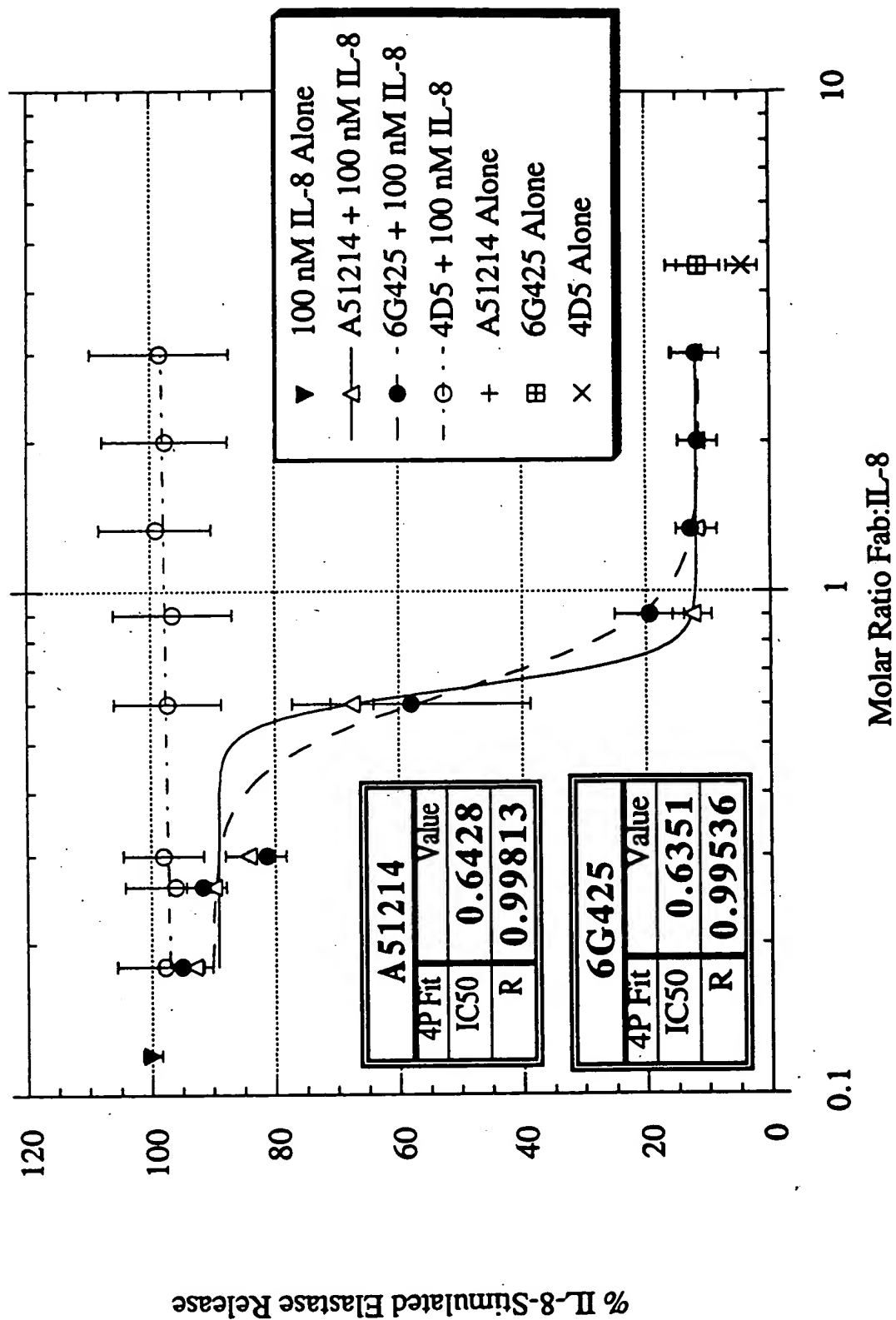
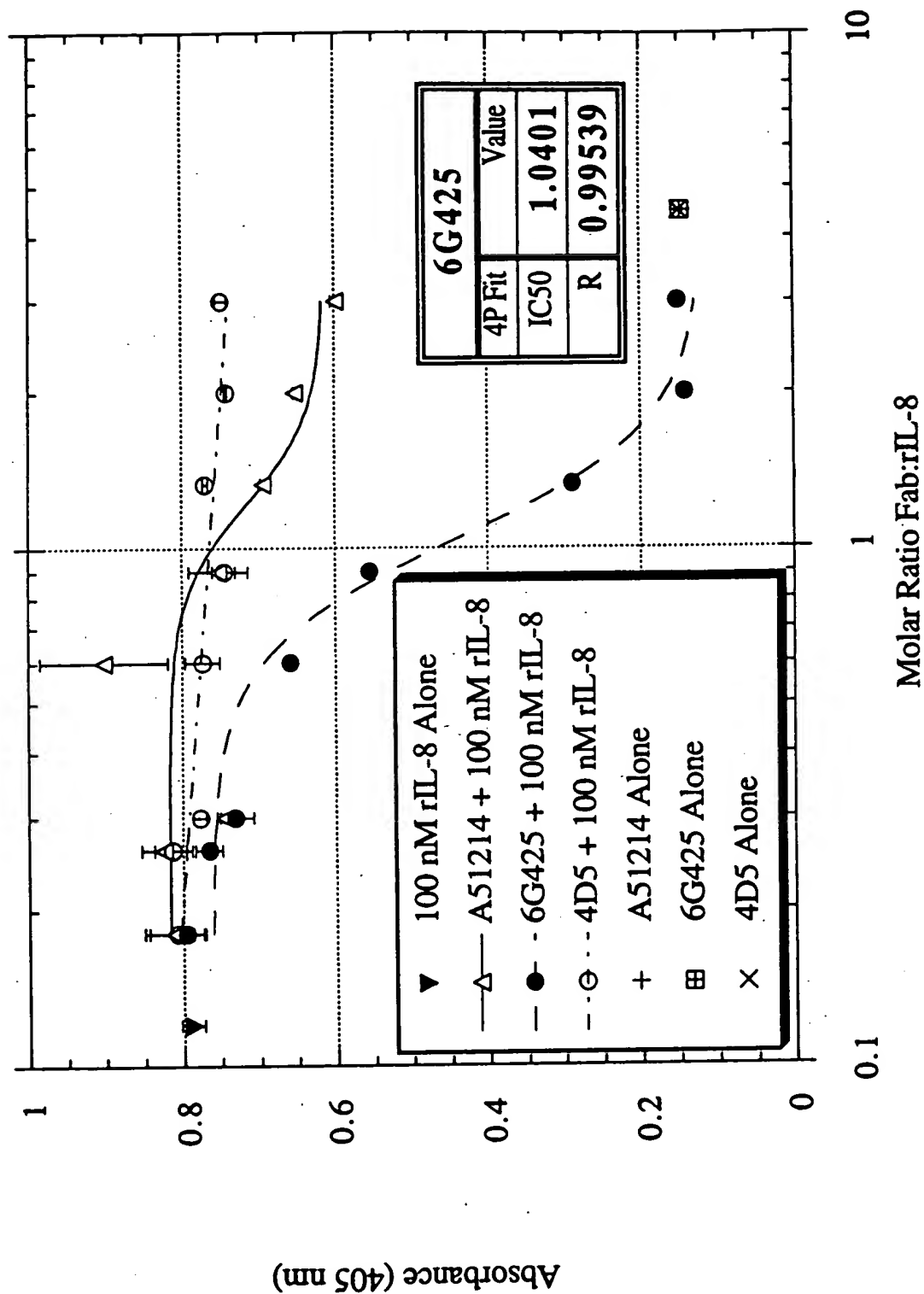


FIG. 10





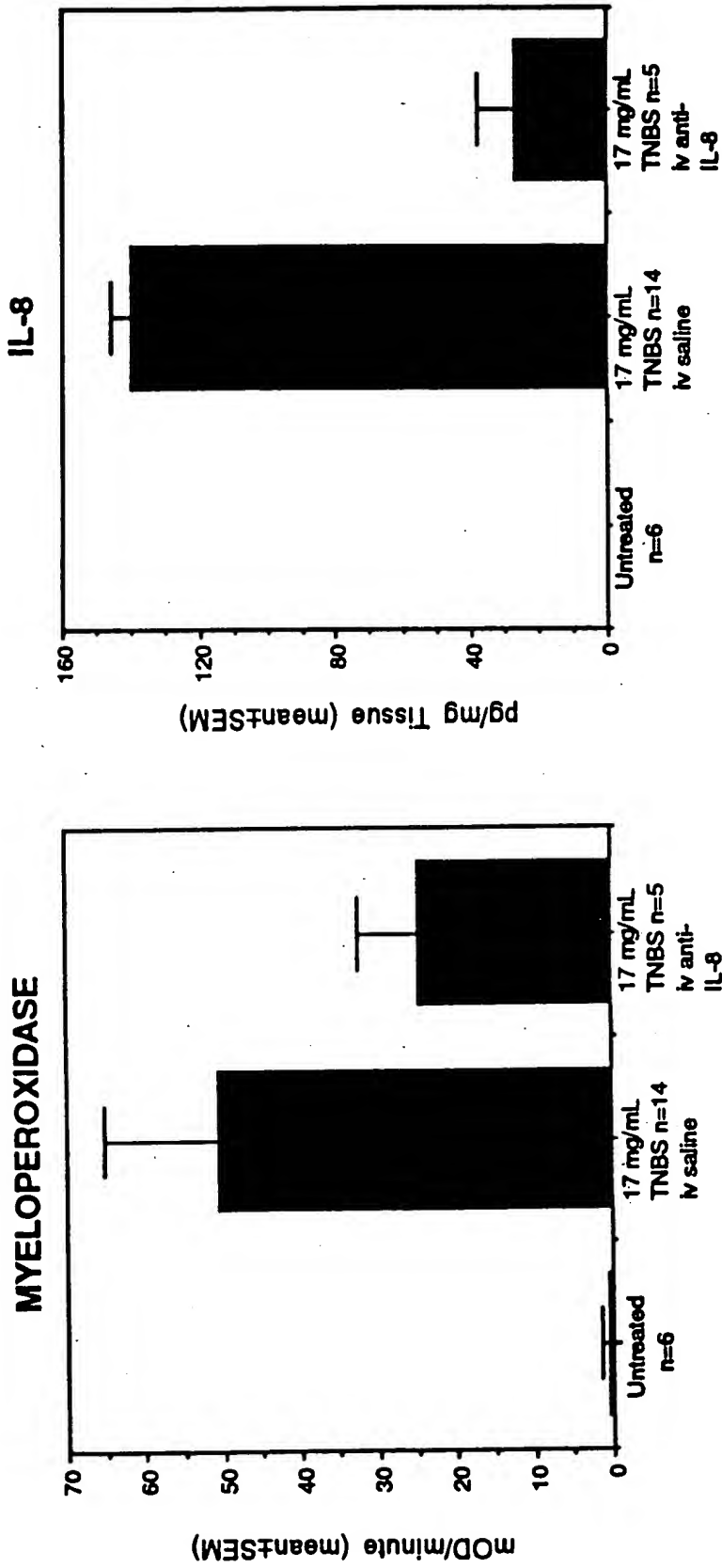


FIG. 11A

FIG. 11B

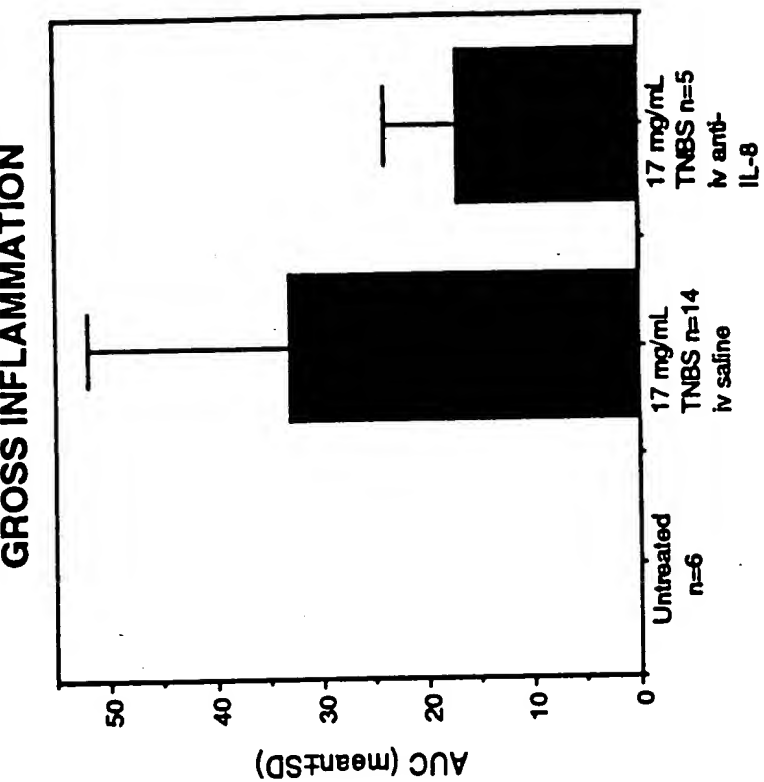


FIG. 11D

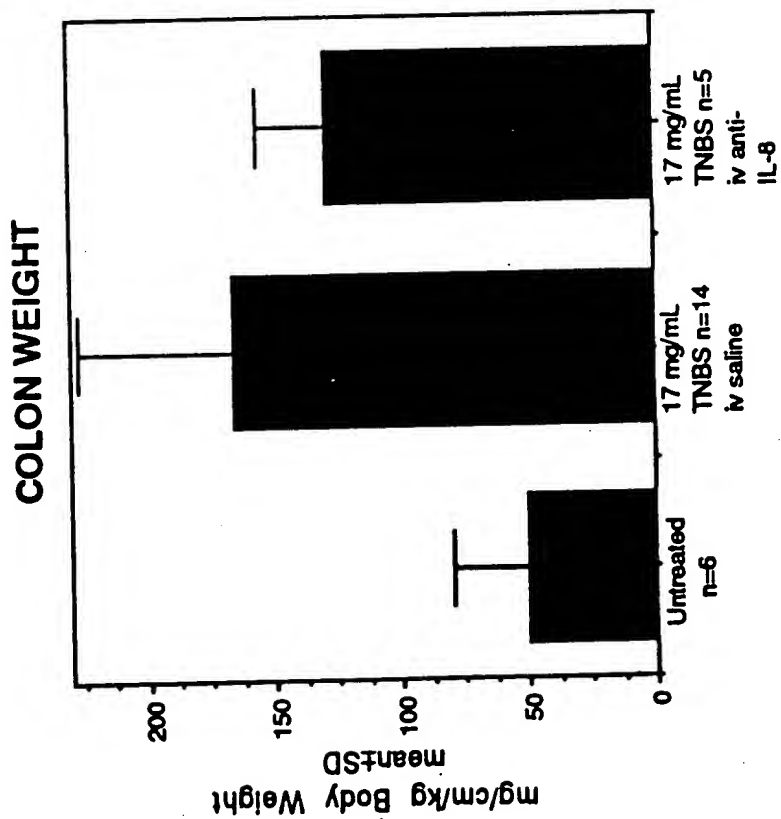


FIG. 11C

# EDEMA

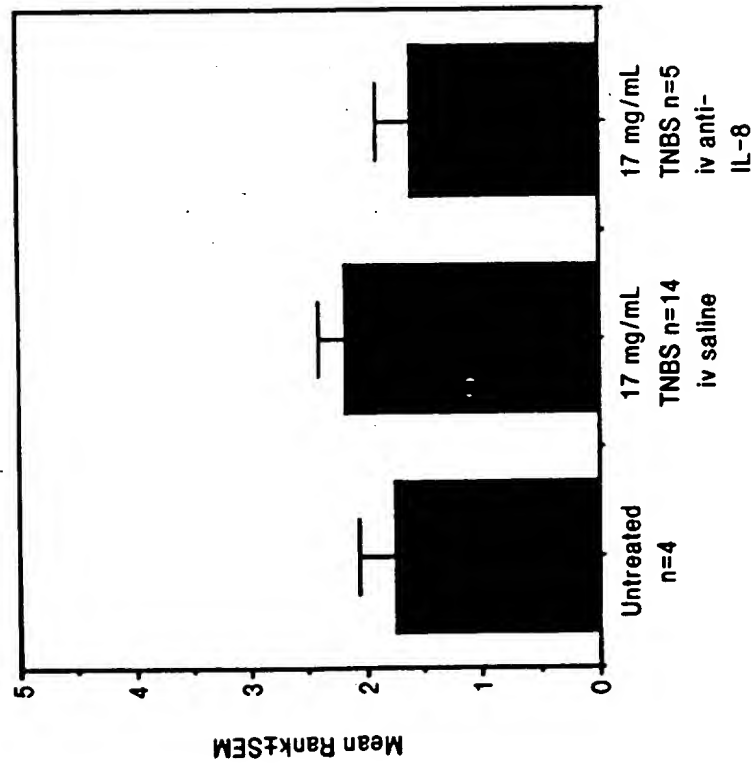


FIG. 11E

# EXTENT OF NECROSIS

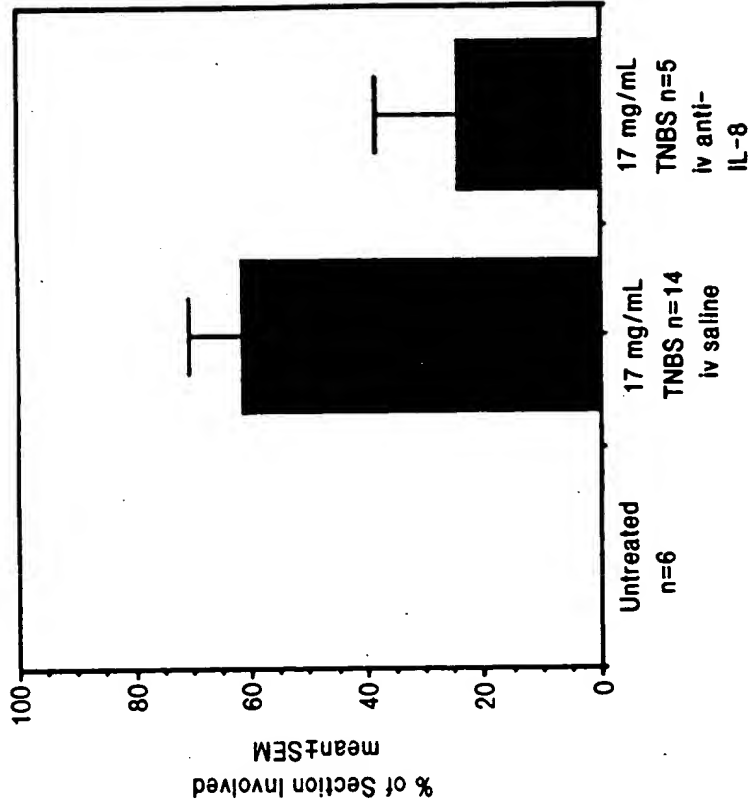
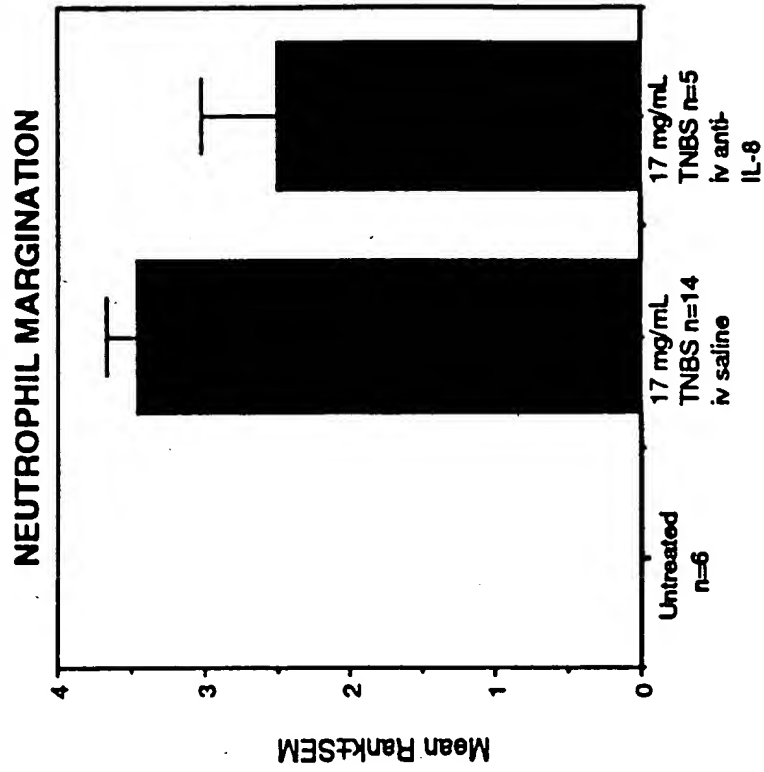
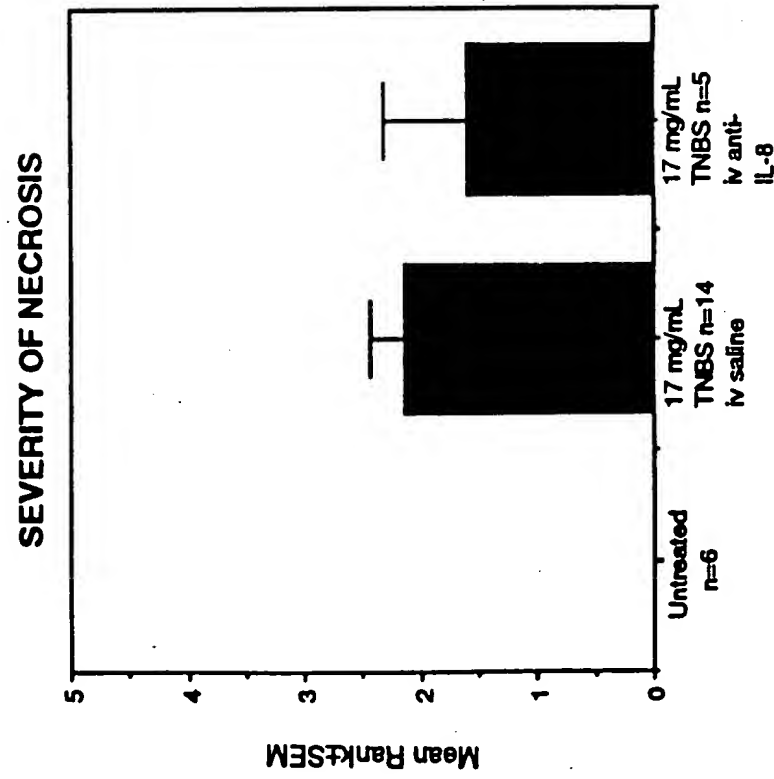


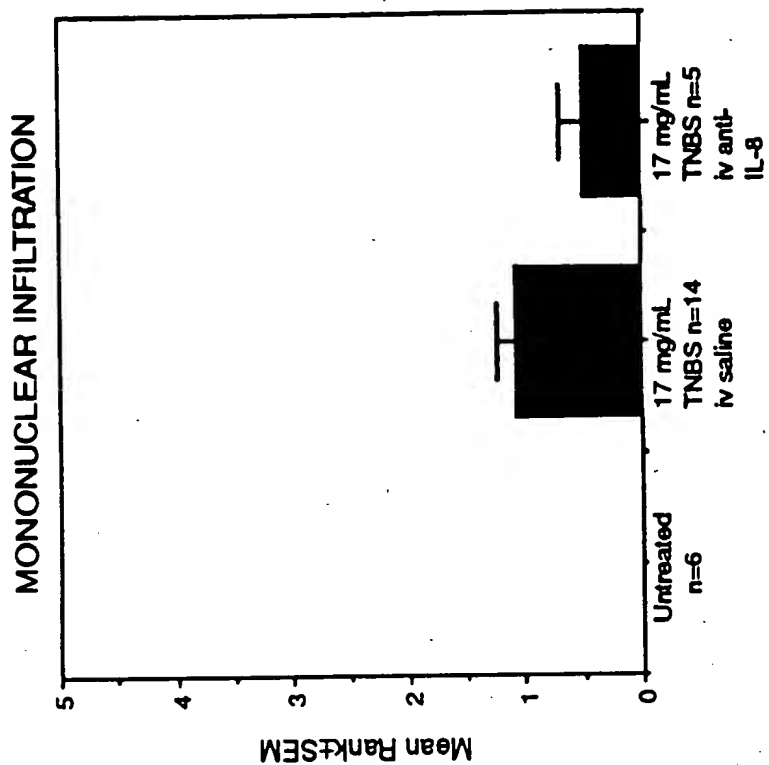
FIG. 11F



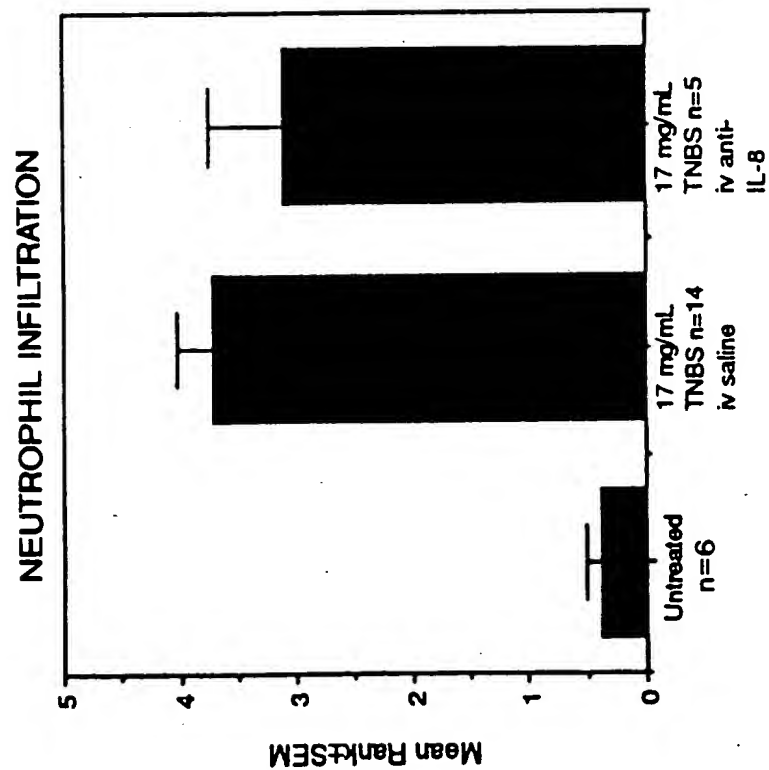
**FIG. 11H**



**FIG. 11G**

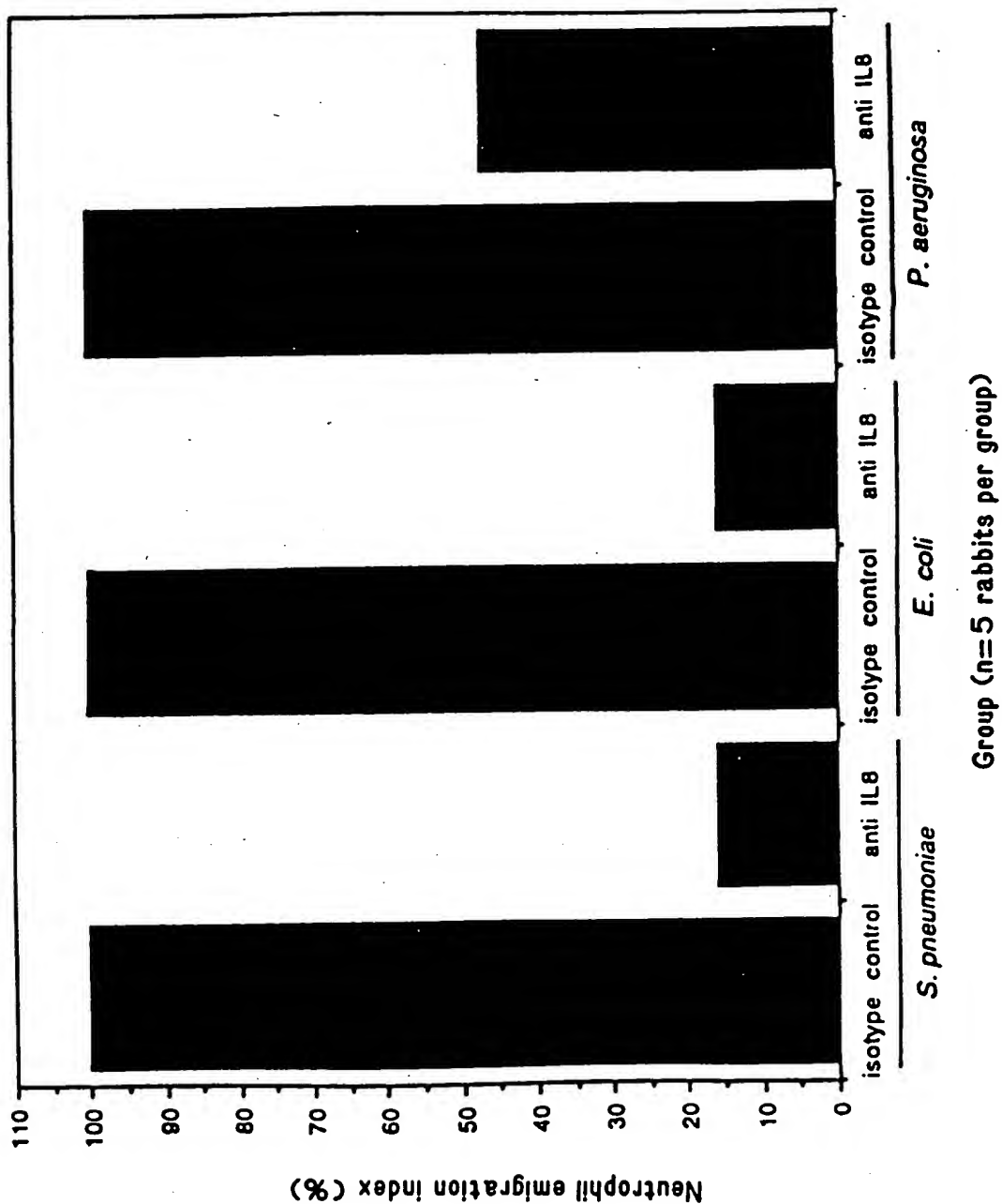


**FIG. 11J**



**FIG. 11I**

FIG. 12



Light Chain Primers:

**FIG. 13**

MKLC-1, 22mer

5' CAGTCCAACGTGTCAGGACGCC 3'

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3'

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3'

## FIG. 14

Light chain forward primer

SL001A-2 35 mer

5' ACAAACGCGTACGCT GACATCGTCATGACCCAGTC 3'  
                                  T  T                  T  
  A

Light chain reverse primer

SL001B 37 mer

5' GCTCTTCGAATG GTGGGAAGATGGATACAGTTGGTGC 3'



Heavy chain forward primer

**FIG. 15**

SL002B 39 mer

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTGGC 3'

T

C

G

A

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTGGC 3'

T

A

G

1 GACATTGTCA TGACACAGTC TCAAAAATTC ATGTCCACAT CAGTAGGAGA CAGGGTCAGC  
CTGTAACAGT ACTGTGTCAG AGTTTTTAAG TACAGGTGTA GTCATCCTCT GTCCCAGTCG  
1 D I V M T Q S Q K F M S T S V G D R V S

61 GTCACCTGCA AGGCCAGTCA GAATGTGGT ACTAATGTAG CCTGGTATCA ACAGAAACCA  
CAGTGGACGT TCCGGTCAGT CTTACACCCA TGATTACATC GGACCATAGT TGTCTTTGGT  
21 V T C K A S O N V G T N V A W Y Q Q K P

CDR #1

121 GGGCAATCTC CTAAAGCACT GATTACTCG TCATCCTACC GGTACAGTGG AGTCCCCTGAT  
CCCGTTAGAG GATTTCGTGA CTAAATGAGC AGTAGGATGG CCATGTCACC TCAGGGACTA  
41 G Q S P K A L I Y S S S Y R Y S G V P D

CDR #2

181 CGCTTCACAG GCAGTGGATC TGGACACAGAT TTCACTCTCA CCATCAGCCA TGTGCAGTCT  
GCGAAGTGTC CGTCACCTAG ACCCTGTCTA AAGTGAGAGT GGTAGTCGGT ACACGTCAGA  
61 R F T G S G S G T D F T L T I S H V Q S

241 GAAGACTTGG CAGACTATTT CTGTCAGCAA TATAACATCT ATCCTCTCAC GTTCGGTCCT  
CTTCTGAACC GTCTGATAAA GACAGTCGTT ATATTGTAGA TAGGAGAGTG CAAGCCAGGA  
81 E D L A D Y F C Q Q Y N I Y P L T F G P

CDR #3

301 GGGACCAAGC TGGAGTTGAA ACGGGCTGAT GCTGCACCAC CAACTGTATC CATCTCCCA  
CCCTGGTTCG ACCTCAACTT TGCCCCGACTA CGACGTGGTG GTTGACATAG GTAGAAGGT  
101 G T K L E L K R A D A A P P T V S I F P

BstBI

361 CCATTTCGAA

GGTAAGCTT

121 P F E

FIG. 16

1 TTCTATTGCT ACAAACGCGT ACGCTGAGGT GCAGCTGGTG GAGTCTGGGG GAGGCTTAGT  
 AAGATAACGA TGTTTGCGCA TGC GACTCCA CGTCGACCAC CTCAGACCCC CTCCGAATCA  
 1 E V Q L V E S G G G L V

61 GCCGCCTGGA GGGTCCCTGA AACTCTCCTG TGCAGCCTCT GGATTTCATAT TCAGTAGTTA  
 CGGCGGACCT CCCAGGGACT TTGAGAGGAC ACGTCGGAGA CCTAAGTATA AGTCATCAAT  
 13 P P G G S L K L S C A A S G F I F S S Y \* \*

CDR #1

121 TGGCATGTCT TGGGTTCGCC AGACTCCAGG CAAGAGCCTG GAGTTGGTCG CAACCATTTAA  
 ACCGTACAGA ACCCAAGCGG TCTGAGGTCC GTTCTCGGAC CTCAACCAGC GTTGGTAATT  
 33 G M S W V R Q T P G K S L E L V A T I N \* \* \*

181 TAATAATGGT GATAGCACCT ATTATCCAGA CAGTGTGAAG GGCCGATTCA CCATCTCCCG  
 ATTATTACCA CTATCGTGGA TAATAGGTCT GTCACACTTC CCGGCTAAGT GGTAGAGGGC  
 53 N N G D S T Y Y P D S V K G R F T I S R \* \* \* \*

CDR #2

241 AGACAATGCC AAGAACACCC TGTACCTGCA AATGAGCAGT CTGAAGTCTG AGGACACAGC  
 TCTGTACCG TTCTTGTTGGG ACATGGACGT TTACTCGTCA GACTTCAGAC TCCTGTGTCG  
 73 D N A K N T L Y L Q M S S L K S E D T A

301 CATGTTTTAC TGTGCAAGAG CCCTCATTAG TTCGGCTACT TGGTTTGGTT ACTGGGGCCA  
 GTACAAAATG ACACGTTCTC GGGAGTAATC AAGCCGATGA ACCAAACCAA TGACCCCGGT  
 93 M F Y C A R A L I S S A T W F G Y W G Q \* \* \* \* \*

CDR #3

361 AGGGACTCTG GTCAGTGTCT CTGCAGCCAA AACAAACAGCC CCATCTGTCT  
 TCCCTGAGAC CAGTGACAGA GACGTCGGTT TTGTTGTCGG GGTAGACAGA  
 113 G T L V T V S A A K T T A P S V Y

ApaI

411 ATCCGGG  
 TAGGCCC  
 130 P

FIG. 17

## FIG. 18

VL.front 31-MER

5' ACAAACGCGTACGCTGATATCGTCATGACAG 3'

VL.rear 31-MER

5' GCAGCATCAGCTCTTCGAAGCTCCAGCTTGG 3'

VH.front.SPE 21-MER

5' CCACTAGTACGCAAGTTCACG 3'

VH.rear 33-MER

5' GATGGGCCCTTGGTGGAGGCTGCAGAGACAGTG 3'

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTCG TTTTCTCTAT TGCTACAAAC  
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG  
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG ATATCGTCAT GACACAGTCT CAAAAATTCA TGTCCACATC AGTAGGAGAC  
CGCATGCGAC TATAGCAGTA CTGTGTCAGA GTTTTAAAGT ACAGGTGTAG TCATCCTCTG  
-3 A Y A D I V M T Q S Q K F M S T S V G D

121 AGGGTCAGCG TCACCTGCAA GGCCAGTCAG AATGTGGGTA CTAATGTAGC CTGGTATCAA  
TCCCAGTCGC AGTGGACGTT CCGGTCAGTC TTACACCCAT GATTACATCG GACCATAGTT  
18 R V S V T C K A S O N V G T N V A W Y Q  
\* \* \* \* \* \* \* \* \*

CDR #1

181 CAGAAACCAG GGCAATCTCC TAAAGCACTG ATTTACTCGT CATCCTACCG GTACAGTGGA  
GTCTTTGGTC CCGTTAGAGG ATTTCTGTGAC TAAATGAGCA GTAGGATGGC CATGTCACTT  
38 Q K P G Q S P K A L I Y S S S Y R Y S G  
\* \* \* \* \*

CDR #2

241 GTCCCTGATC GCTTCACAGG CAGTGGATCT GGGACAGATT TCACTCTCAC CATCAGCCAT  
CAGGGACTAG CGAAGTGTCC GTCACCTAGA CCCTGTCTAA AGTGAGAGTG GTAGTCGGTA  
58 V P D R F T G S G S G T D F T L T I S H

301 GTGCAGTCTG AAGACTTGGC AGACTATTTT TGTCAGCAAT ATAACATCTA TCCTCTCAGC  
CACGTCAGAC TTCTGAACCG TCTGATAAAG ACAGTCGTTA TATTGTAGAT AGGAGAGTGC  
78 V Q S E D L A D Y F C Q Q Y N I Y P L T  
\* \* \* \* \*

CDR #3

BstBI

361 TTCGGTCCTG GGACCAAGCT GGAGCTTTCGA AGAGCTGTGG CTGCACCATC TGTCTTCATC  
AAGCCAGGAC CCTGGTTCGA CCTCGAAGCT TCTCGACACC GACGTGGTAG ACAGAAGTAG  
98 F G P G T K L E L R R A V A A P S V F I

421 TTCCCGCCAT CTGATGAGCA GTTGAAATCT GGAAGTCTT CTGTTGTGTG CCTGCTGAAT  
AAGGGCGGTA GACTACTCGT CAACTTTAGA CCTTGACGAA GACAACACAC GGACGACTTA  
118 F P P S D E Q L K S G T A S V V C L L N

481 AACTTCTATC CCAGAGAGGC CAAAGTACAG TGGAAGGTGG ATAACGCCCT CCAATCGGGT  
TTGAAGATAG GGTCTCTCCG GTTTCATGTC ACCTTCCACC TATTGCGGGA GGTTAGCCCA  
138 N F Y P R E A K V Q W K V D N A L Q S G

541 AACTCCCAGG AGAGTGTAC AGAGCAGGAC AGCAAGGACA GCACCTACAG CCTCAGCAGC  
TTGAGGGTCC TCTCACAGTG TCTCGTCTG TCGTTCCTGT CGTGGATGTC GGAGTCGTCG  
158 N S Q E S V T E Q D S K D S T Y S L S S

601 ACCCTGACGC TGAGCAAAGC AGACTACGAG AAACACAAAG TCTACGCCTG CGAAGTCACC  
TGGGACTGCG ACTCGTTTTC TCTGATGCTC TTTGTGTTTC AGATGCGGAC GCTTCAGTGG  
178 T L T L S K A D Y E K H K V Y A C E V T

661 CATCAGGGCC TGAGCTCGCC CGTCACAAAG AGCTTCAACA GGGGAGAGTG  
GTAGTCCCGG ACTCGAGCGG GCAGTGTTC TCGAAGTTGT CCCCTCTCAC  
198 H Q G L S S P V T K S F N R G E C

711 TTAA  
AATT  
216 O

FIG. 19

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC  
TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG  
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGGTGCAGCT GGTGGAGTCT GGGGGAGGCT TAGTGCCGCC TGGAGGGTCC  
CGCATGCGAC TCCACGTCGA CCACCTCAGA CCCCCTCCGA ATCACGGCGG ACCTCCCAGG  
-3 A Y A E V Q L V E S G G G L V P P G G S

121 CTGAAACTCT CCTGTGCAGC CTCTGGATTTC ATATTCAGTA GTTATGGCAT GTCTTGGGTT  
GACTTTGAGA GGACACGTCG GAGACCTAAG TATAAGTCAT CAATACCGTA CAGAACCCAA  
18 L K L S C A A S G F I F S S Y G M S W V  
\* \* \* \*

CDR #1

181 CGCCAGACTC CAGGCAAGAG CCTGGAGTTG GTCGCAACCA TTAATAATAA TGGTGATAGC  
GCGGTCTGAG GTCCGTTCTC GGACCTCAAC CAGCGTTGGT AATTATTATT ACCACTATCG  
38 R Q T P G K S L E L V A T I N N N G D S  
\* \* \* \* \*

241 ACCTATTATC CAGACAGTGT GAAGGGCCGA TTCACCATCT CCCGAGACAA TGCCAAGAAC  
TGGATAATAG GTCTGTCACA CTTCCTCGGCT AAGTGGTAGA GGGCTCTGTT ACGGTTCTTG  
58 T Y Y P D S V K G R F T I S R D N A K N  
\* \* \* \* \*

CDR #2

301 ACCCTGTACC TGCAAATGAG CAGTCTGAAG TCTGAGGACA CAGCCATGTT TTAAGTGTGCA  
TGGGACATGG ACGTTTACTC GTCAGACTTC AGACTCCTGT GTCGGTACAA AATGACACGT  
78 T L Y L Q M S S L K S E D T A M F Y C A

361 AGAGCCCTCA TTAGTTCGGC TACTTGGTTT GGTTACTGGG GCCAAGGGAC TCTGGTCACT  
TCTCGGGAGT AATCAAGCCG ATGAACCAAA CCAATGACCC CGGTTCCCTG AGACCAAGTGA  
98 R A L I S S A T W F G Y W G Q G T L V T  
\* \* \* \* \*

CDR #3

ApaI

421 GTCTCTGCAG CCTCCACCAA GGGCCCATCG GTCTTCCCCC TGGCACCCCTC CTCCAAGAGC  
CAGAGACGTC GGAGGTGGTT CCCGGGTAGC CAGAAGGGGG ACCGTGGGAG GAGGTTCTCG  
118 V S A A S T K G P S V F P L A P S S K S

481 ACCTCTGGGG GCACAGCGGC CCTGGGCTGC CTGGTCAAGG ACTACTTCCC CGAACCGGTG  
TGGAGACCCC CGTGTCGCCC GGACCCGACG GACCAGTTCC TGATGAAGGG GCTTGGCCAC  
138 T S G G T A A L G C L V K D Y F P E P V

541 ACGGTGTCGT GGAACCTCAGG CGCCCTGACC AGCGGCGTGC ACACCTTCCC GGCTGTCCTA  
TGCCACAGCA CCTTGAGTCC GCGGGACTGG TCGCCGCACG TGTGGAAGGG CCGACAGGAT  
158 T V S W N S G A L T S G V H T F P A V L

601 CAGTCCTCAG GACTCTACTC CCTCAGCAGC GTGGTGACCG TGCCCTCCAG CAGCTTGGGC  
GTCAGGAGTC CTGAGATGAG GGAGTCGTCG CACCACTGGC ACGGGAGGTC GTCGAACCCG  
178 Q S S G L Y S L S S V V T V P S S S L G

FIG. 20A

661 ACCCAGACCT ACATCTGCAA CGTGAATCAC AAGCCCAGCA ACACCAAGGT GGACAAGAAA  
TGGGTCTGGA TG TAGACGTT GCACTTAGTG TTCGGGTCGT TGTGGTTCCA CCTGTTCTTT  
198 T Q T Y I C N V N H K P S N T K V D K K  
721 GTTGAGCCCA AATCTTGTGA CAAAACAC ACATGA  
CAACTCGGGT TTAGAACACT GTTTGAGTG TGTACT  
218 V E P K S C D K T H T O

FIG. 20B

Light Chain Primers:

MKLC-1, 22mer

5' CAGTCCAAGTGTTCAGGACGCC 3'

MKLC-2, 22mer

5' GTGCTGCTCATGCTGTAGGTGC 3'

MKLC-3, 23mer

5' GAAGTTGATGTCTTGTGAGTGGC 3'

Heavy Chain Primers:

IGG2AC-1, 24mer

5' GCATCCTAGAGTCACCGAGGAGCC 3'

IGG2AC-2, 22mer

5' CACTGGCTCAGGGAAATAACCC 3'

IGG2AC-3, 22mer

5' GGAGAGCTGGGAAGGTGTGCAC 3'

**FIG. 21**



Light chain forward primer

6G4.light.Nsi 36-MER

5' CCAATGCATACGCT GAC ATC GTG ATG ACC CAG ACC CC 3'  
                          T   T                  T          T  
  A          A

Light chain reverse primer

6G4.light.Mun 35-MER

5' AGA TGT CAA TTG CTC ACT GGA TGG TGG GAA GAT GG 3'

**FIG. 22**

Heavy chain forward primer

6G4.heavy.Mlu 32-MER

5' CAAACGCGTACGCT GAG ATC CAG CTG CAG CAG 3'  
  T                  C

Heavy chain reverse primer

SL002B 39-MER

5' CGATGGGCCCCG ATAGACCGATGGGGCTGTTGTTTTGGC 3'  
  T  
  A  
  G

**FIG. 23**

70 G ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT  
 C TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA  
 1 D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGTCAG ATCTAGTCAG AGCCTTGTAC ACGGTATTGG AAACACCTAT  
 GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA  
 18 Q A S I S C R S S O S L V H G I G N T Y  
 \* \* \* \* \*  
 CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC  
 AATGTAACCA TGGACGTCTT CCGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG  
 38 L H W Y L Q K P G Q S P K L L I Y K V S  
 \* \* \* \* \*  
 CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTC AGTGGCAGTG GATCAGGGAC AGATTTTCACA  
 TTGGCTAAAA GACCCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT  
 58 N R F S G V P D R F S G S G S G T D F T  
 \* \* \* \* \*

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA  
 GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT  
 78 L R I S R V E A E D L G L Y F C S Q S T  
 \* \* \* \* \*  
 CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGATGCTGCA  
 GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCC ACTACGACGT  
 98 H V P L T F G A G T K L E L K R A D A A  
 \* \* \* \* \*

MunI

421 CCAACTGTAT CCATCTTCCC ACCATCCAGT GAGCAATTGA  
 GGTGACATA GGTAGAAGGG TGGTAGGTCA CTCGTAACT  
 118 P T V S I F P P S S E Q L K

FIG. 24

70 G AGATTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA  
 C TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT  
 1 E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTGAGTA GCCACTACAT GCACTGGGTG  
 CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC  
 18 V K I S C K A S G Y S F S S H Y M H W V  
 \* \* \* \* \*

CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA  
 TTCGTCTCGG TACCTTTCTC GGAAGTCACC TAACCGATGT AACTAGGAAG GTTACCACTT  
 38 K Q S H G K S L E W I G Y I D P S N G E  
 \* \* \* \* \*

CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC  
 TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAC TACATCTGTG TAGAAGGTGG  
 58 T T Y N Q K F K G K A T L T V D T S S S  
 \* \* \* \* \*

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA  
 TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT  
 78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG  
 TCTCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC  
 98 R G D Y R Y N G D W F F D V W G A G T T  
 \* \* \* \* \*

CDR #3

BstEII
 ApaI

421 GTCACCGTCT CCTCCGCCAA AACCGACAGC CCCATCGGTC TATCCGGGGCC  
 CAGTGCCAGA GGAGGCGGAT TTGGCTGTCT GGGTAGCCAG ATAGGCCCCG  
 118 V T V S S A K T D S P I G L S G P

471 CATC  
 GTAG  
 135 I

FIG. 25

5' CTTGGTGGAGGCGGAGGAGACG 3'

Mutagenesis Primer for 6G425VL

DS/VF 38MER

5' GAAACGGGCTGTTGCTGCACCAACTGTATTCATCTTCC 3'

SYN.BstEII 31 MER

5' GTCACCGTCT CCTCCGCCTC CACCAAGGGC C 3'

SYN.Apa 22 MER

5' CTTGGTGGAGGCGGAGGAGACG 3'

**FIG. 26**

1 ATGAAGAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAT  
TACTTCTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTA  
-23 M K K N I A F L L A S M F V F S I A T N

61 GCATACGCTG ATATCGTGAT GACACAGACA CCACTCTCCC TGCCTGTCAG TCTTGGAGAT  
CGTATGCGAC TATAGCACTA CTGTGTCTGT GGTGAGAGGG ACGGACAGTC AGAACCTCTA  
-3 A Y A D I V M T Q T P L S L P V S L G D

121 CAGGCCTCCA TCTCTTGCA G ATCTAGTCAG AGCCTTGATC ACGGTATTGG AAACACCTAT  
GTCCGGAGGT AGAGAACGTC TAGATCAGTC TCGGAACATG TGCCATAACC TTTGTGGATA  
18 Q A S I S C R S S O S L V H G I G N T Y  
\* \* \* \* \* \* \* \* \* \* \* \* \*

CDR #1

181 TTACATTGGT ACCTGCAGAA GCCAGGCCAG TCTCCAAAGC TCCTGATCTA CAAAGTTTCC  
AATGTAACCA TGGACGTCTT CCGTCCGGTC AGAGGTTTCG AGGACTAGAT GTTTCAAAGG  
38 L H W Y L Q K P G Q S P K L L I Y K V S  
\* \* \* \* \*

CDR #2

241 AACCGATTTT CTGGGGTCCC AGACAGGTTT AGTGGCAGTG GATCAGGGAC AGATTTCACA  
TTGGCTAAAA GACCCAGGG TCTGTCCAAG TCACCGTCAC CTAGTCCCTG TCTAAAGTGT  
58 N R F S G V P D R F S G S G S G T D F T  
\* \* \* \*

301 CTCAGGATCA GCAGAGTGGA GGCTGAGGAT CTGGGACTTT ATTTCTGCTC TCAAAGTACA  
GAGTCCTAGT CGTCTCACCT CCGACTCCTA GACCCTGAAA TAAAGACGAG AGTTTCATGT  
78 L R I S R V E A E D L G L Y F C S Q S T  
\* \* \* \*

CDR #3

361 CATGTTCCGC TCACGTTCGG TGCTGGGACC AAGCTGGAGC TGAAACGGGC TGTTGCTGCA  
GTACAAGGCG AGTGCAAGCC ACGACCCTGG TTCGACCTCG ACTTTGCCCG ACAACGACGT  
98 H V P L T F G A G T K L E L K R A V A A  
\* \* \* \*

421 CCAACTGTAT TCATCTTCCC ACCATCCAGT GAGCAATTGA AATCTGGAAC TGCCTCTGTT  
GGTTGACATA AGTAGAAGGG TGGTAGGTCA CTCGTTAAC TTAGACCTTG ACGGAGACAA  
118 P T V F I F P P S S E Q L K S G T A S V

481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGA GGTGGATAAC  
CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG  
138 V C L L N N F Y P R E A K V Q W K V D N

541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC  
CGGGAGGTTA GCCCATGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTT  
158 A L Q S G N S Q E S V T E Q D S K D S T

601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC  
ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG  
178 Y S L S S T L T L S K A D Y E K H K V Y

FIG. 27A

CGGACGCTTC AGTGGGTAGT

661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA  
CGGACGCTTC AGTGGGTAGT CCGGACTCG AGCGGCAGT GTTCTCGAA GTTGTCCTT  
198 A C E V T H Q G L S S P V T K S F N R G

721 GAGTGTAA  
CTCACAATT  
218 E C O

FIG. 27B

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC  
TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATAACAAGC AAAAAAGATA ACGATGTTTG  
-23 M K K N I A F L L A S M F V F S I A T N

61 GCGTACGCTG AGATTTCAGCT GCAGCAGTCT GGACCTGAGC TGATGAAGCC TGGGGCTTCA  
CGCATGCGAC TCTAAGTCGA CGTCGTCAGA CCTGGACTCG ACTACTTCGG ACCCCGAAGT  
-3 A Y A E I Q L Q Q S G P E L M K P G A S

121 GTGAAGATAT CCTGCAAGGC TTCTGGTTAT TCATTTCAGTA GCCACTACAT GCACTGGGTG  
CACTTCTATA GGACGTTCCG AAGACCAATA AGTAAGTCAT CGGTGATGTA CGTGACCCAC  
18 V K I S C K A S G Y S F S S H Y M H W V  
\* \* \* \*

#### CDR #1

181 AAGCAGAGCC ATGGAAAGAG CCTTGAGTGG ATTGGCTACA TTGATCCTTC CAATGGTGAA  
TTCGTCTCGG TACCTTTCTC GGAACCTCACC TAACCGATGT AACTAGGAAG GTTACCACTT  
38 K Q S H G K S L E W I G Y I D P S N G E  
\* \* \* \* \*

#### CDR #2

241 ACTACTTACA ACCAGAAATT CAAGGGCAAG GCCACATTGA CTGTAGACAC ATCTTCCAGC  
TGATGAATGT TGGTCTTTAA GTTCCCGTTC CGGTGTAAC TACATCTGTG TAGAAGGTGC  
58 T T Y N Q K F K G K A T L T V D T S S S  
\* \* \* \* \*

301 ACAGCCAACG TGCATCTCAG CAGCCTGACA TCTGATGACT CTGCAGTCTA TTTCTGTGCA  
TGTCGGTTGC ACGTAGAGTC GTCGGACTGT AGACTACTGA GACGTCAGAT AAAGACACGT  
78 T A N V H L S S L T S D D S A V Y F C A

361 AGAGGGGACT ATAGATACAA CGGCGACTGG TTTTTCGATG TCTGGGGCGC AGGGACCACG  
TCTCCCCTGA TATCTATGTT GCCGCTGACC AAAAAGCTAC AGACCCCGCG TCCCTGGTGC  
98 R G D Y R Y N G D W F F D V W G A G T T  
\* \* \* \* \*

#### CDR #3

421 GTCACCGTCT CCTCCGCCTC CACCAAGGGC CCATCGGTCT TCCCCCTGGC ACCCTCCTCC  
CAGTGGCAGA GGAGGCGGAG GTGGTTCCCG GGTAGCCAGA AGGGGGACCG TGGGAGGAGG  
118 V T V S S A S T K G P S V F P L A P S S

481 AAGAGCACCT CTGGGGGCAC AGCGGCCCTG GGCTGCCTGG TCAAGGACTA CTTCCTCCGAA  
TTCTCGTGGA GACCCCGGTG TCGCCGGGAC CCGACGGACC AGTTCCTGAT GAAGGGGCTT  
138 K S T S G G T A A L G C L V K D Y F P E

541 CCGGTGACGG TGTCGTGGAA CTCAGGCGCC CTGACCAGCG GCGTGCACAC CTTCCTCCGCT  
GGCCACTGCC ACAGCACCTT GAGTCCGCGG GACTGGTCGC CGCACGTGTG GAAGGGCCGA  
158 P V T V S W N S G A L T S G V H T F P A

601 GTCCTACAGT CCTCAGGACT CTACTCCCTC AGCAGCGTGG TGACCGTGCC CTCCAGCAGC  
CAGGATGTCA GGAGTCCTGA GATGAGGGAG TCGTCGCACC ACTGGCACGG GAGGTCGTGC  
178 V L Q S S G L Y S L S S V V T V P S S S

FIG. 28A



661 TTGGGCACCC AGACCTACAT CTGCAACGTG AATCACAAGC CCAGCAACAC CAAGGTGGAC  
 AACCCGTGGG TCTGGATGTA GACGTGTCAC TTAGTGTTTCG GGTGTTGTG GTTCCACCTG  
 198 L G T Q T Y I C N V N H K P S N T K V D  
 721 AAGAAAGTTG AGCCCAAATC TTGTGACAAA ACTCACACAT GA  
 TTCCTTCAAC TCGGGTTAG AACACTGTTT TGAGTGTGTA CT  
 218 K K V E P K S C D K T H T O

FIG. 28B

## Variable Light Chain Domain

	10	20	abcde	30	40
<b>6G425</b>	DIVMTQTPLSLPVSLGDQASISCRSSQSLVHGIGNTYLHWYLQKPGQSPKLLIY				
	# # # # # # # # # # # # # # # #				
<b>F(ab)-1</b>	DIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGNTYLHWYQQKPGKAPKLLIY				
	# # # # # # # # # #				
<b>humkI</b>	DIQMTQSPSSLSASVGDRVTITCRASKTI-----SKYLAWYQQKPGKAPKLLIY				
	=====				
	+++++				
	L1				

	50	60	70	80	90	100
<b>6G425</b>	YKVSNRFGVDPDRFSDSGSGTDFTLRISRVEAEDLGLYFCSQSTHVPLTFGAGTKLELKR					
	# # # # # # # # # # # # # # # #					
<b>F(ab)-1</b>	YKVSNRFGVPSRFRSGSGSGTDFTLTISLQPEDFATYYCSQSTHVPLTFGQGTKVEIKR					
	# # # # # # # # # # # # # # # #					
<b>humkI</b>	YSGSTLESQVPSRFRSGSGSGTDFTLTISLQPEDFATYYCQQHNEYPLTFGQGTKVEIKR					
	===					
	+++++					
	L2			L3		

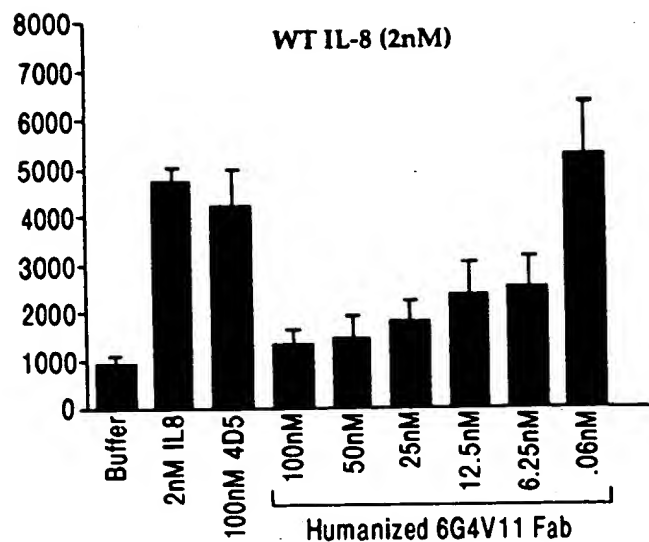
## Variable Heavy Chain Domain

	10	20	30	40
<b>6G425</b>	EIQLQQSGPELMKPGASVKISCKASGYFSSHYMHVWKQSHGKSLEWI			
	# # # # # # # # # # # # # # # #			
<b>F(ab)-1</b>	EVQLVESGGGLVQPGGSLRLSCAASGYFSSHYMHVWRQAPGKGLEWV			
	# # # # #			
<b>humIII</b>	EVQLVESGGGLVQPGGSLRLSCAASGFSFTGHWMNWRQAPGKGLEWV			
	=====			
	+++++			
	H1			

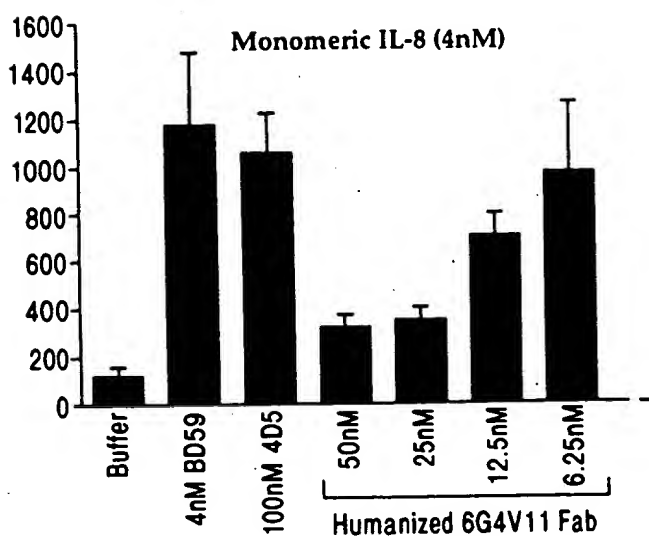
	50	a	70	80	abc	90	100	110
<b>6G425</b>	GYIDPSNGETTYNQKFKGKATLTVDTSSTANVHLSSLTSDDSAVYFCAARGDYRYNGDWFFDVWGAGT							
	# # # # # # # # # # # # # # # #							
<b>F(ab)-1</b>	GYIDPSNGETTYNQKFKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAARGDYRYNGDWFFDVWGQGT							
	# # # # # # # # # # # # # # # #							
<b>humIII</b>	GMIHPSDSETRYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAARGIYFY-GTTYFDYWQGT							
	=====							
	+++++							
	H2				H3			

FIG. 29



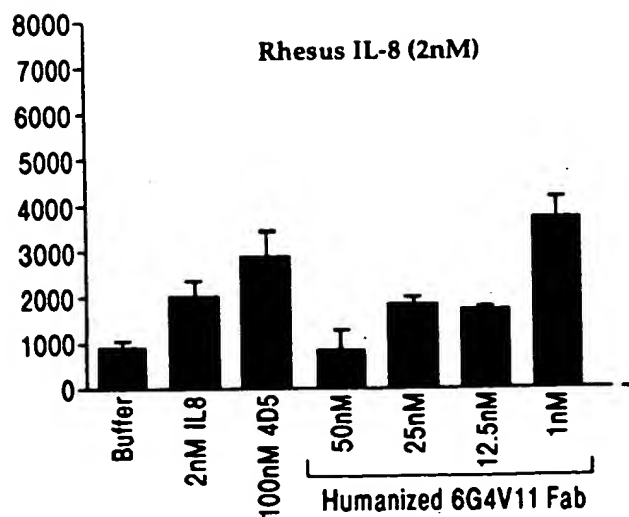
**FIG. 30A**

IC50~12nM



**FIG. 30B**

IC50~15nM



**FIG. 30C**

IC50~22nM

FIG. 31A

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC  
 TACTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG  
 -23 M K K N I A F L L A S M F V F S I A T N  
  
 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT  
 CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA  
 -3 A Y A D I Q M T Q S P S S L S A S V G D  
  
 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TAACACGTAT  
 TCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA  
 18 R V T I T C R S S Q S L V H G I G N T Y  
  
 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC  
 AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG  
 38 L H W Y Q Q K P G K A P K L L I Y K V S  
  
 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT  
 TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA  
 58 N R F S G V P S R F S G S G S G T D F T  
  
 301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT  
 GACTGGTAGT CGTCAGACGT CCGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA  
 78 L T I S S L Q P E D F A T Y Y C S Q S T  
  
 361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA  
 GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT  
 98 H V P L T F G Q G T K V E I K R T V A A  
  
 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT  
 GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA  
 118 P S V F I F P P S D E Q L K S G T A S V  
  
 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC  
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG  
 138 V C L L N N F Y P R E A K V Q W K V D N  
  
 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC  
 CGGGAGGTGA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTT  
 158 A L Q S G N S Q E S V T E Q D S K D S T  
  
 601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC  
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG  
 178 Y S L S S T L T L S K A D Y E K H K V Y  
  
 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA  
 CGGACGCTTC AGTGGGTAGT CCCGACTCG AGCGGGCAGT GTTCTCGAA GTTGTCCCCT  
 198 A C E V T H Q G L S S P V T K S F N R G  
  
 721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA  
 CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT  
 218 E C O

FIG. 31B

**Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Light Chain**

MKKNI AFLLASMFVFSIATNAYADIQMTQSPSSLSASVGDRTITCRSSQSLVHGIGNTY  
LHWYQQKPGKAPKLLIYKVSNRFSGVPSRFSGSGGDTFTLTISLQPEDFAITYCSQST  
HVPLTFGQGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDN  
ALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG  
EC

**Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V19 Heavy Chain**

MKKNI AFLLASMFVFSIATNAYAEVQLVESGGGLVQPGGSLRLSCAASGYSFSSHYMH  
WVKQAPGKGLEWVGVIDPSNGETTYNQFKGRFTLSRDNSKNTAYLQMNSLRAEDTAVYY  
CARGDYRYNGDWFFDVWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYF  
PEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHNKPSNTK  
VDKKVEPKSCDKTHT

**FIG. 31C**



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FIG.32

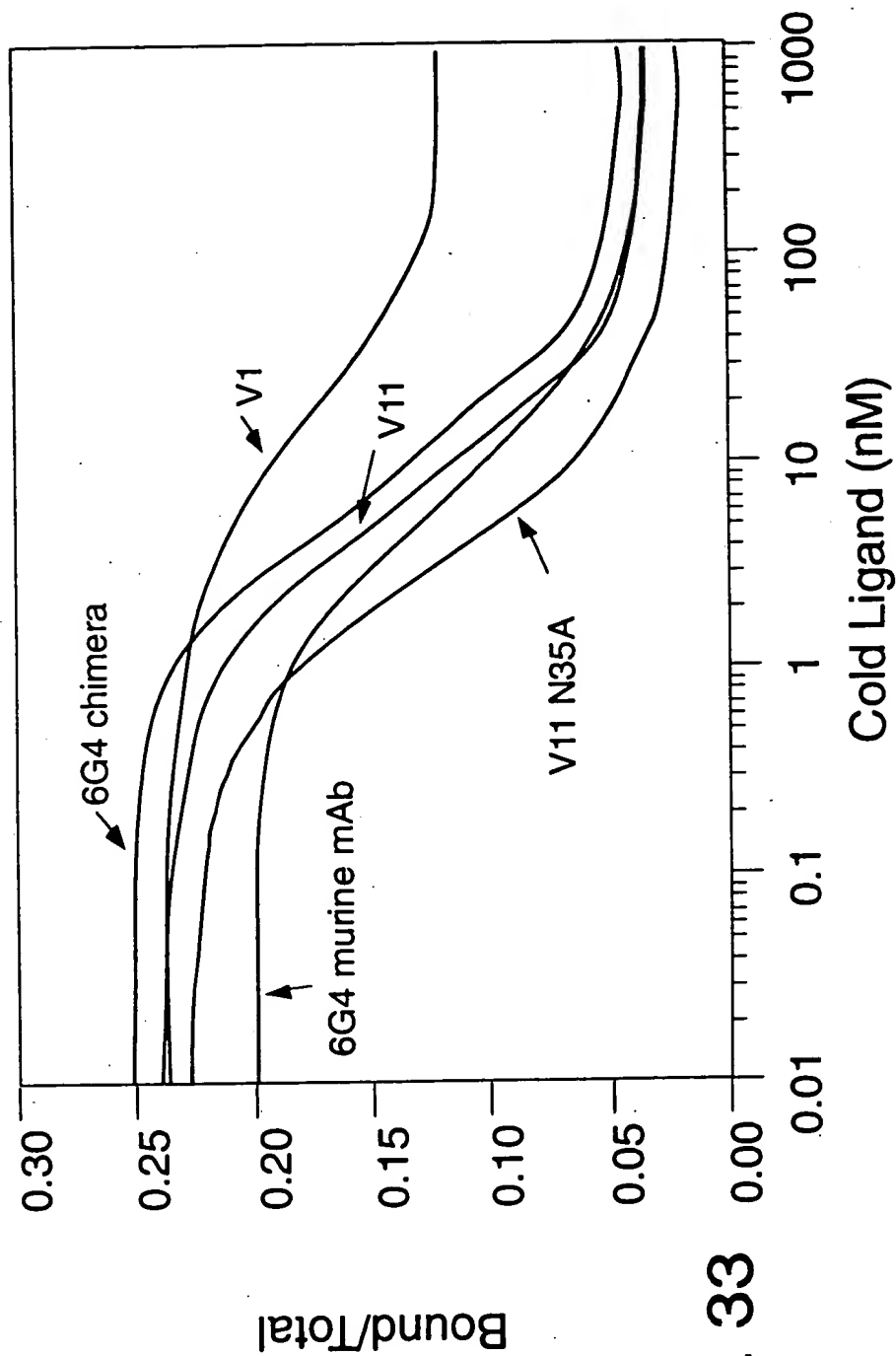
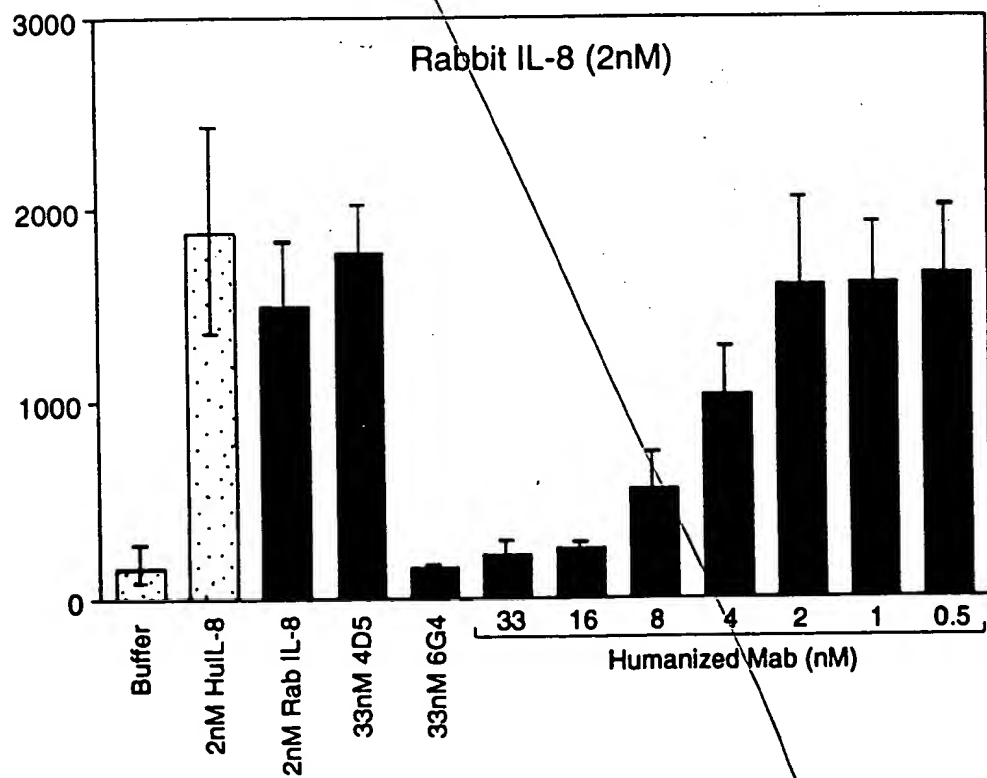
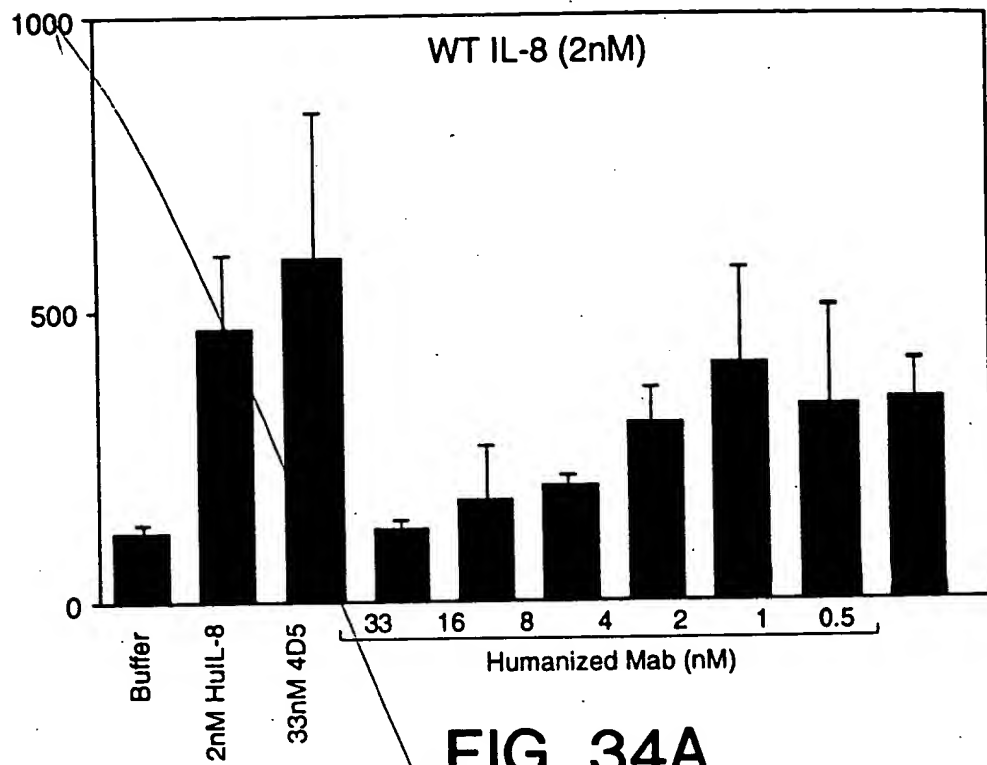
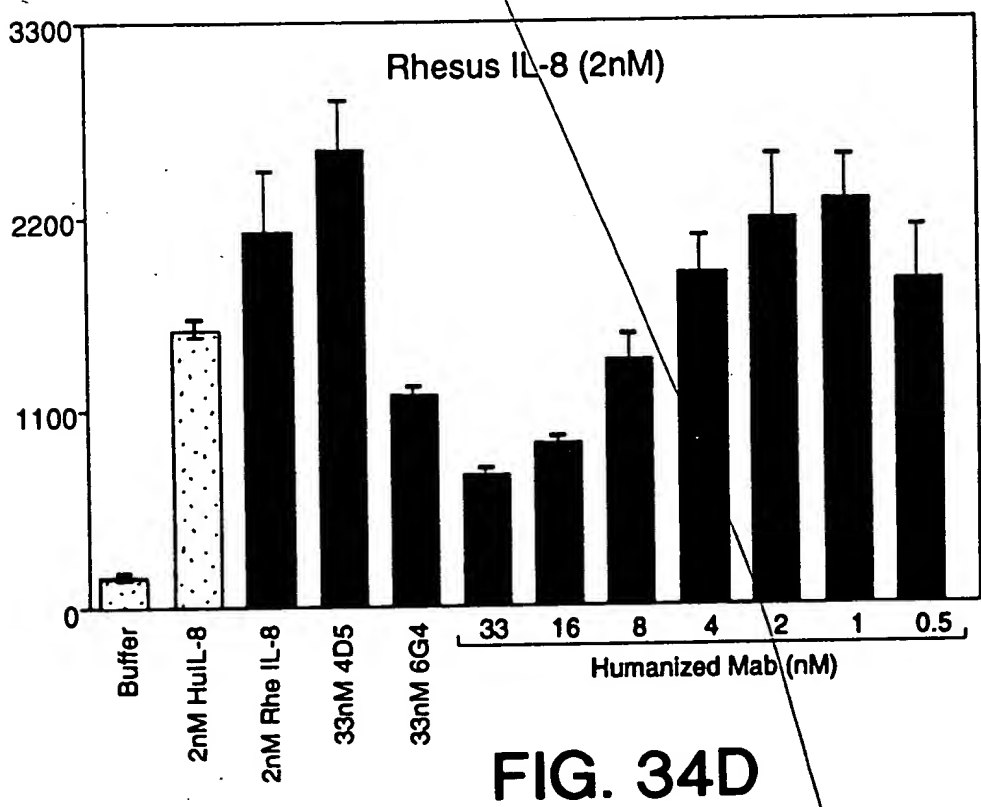
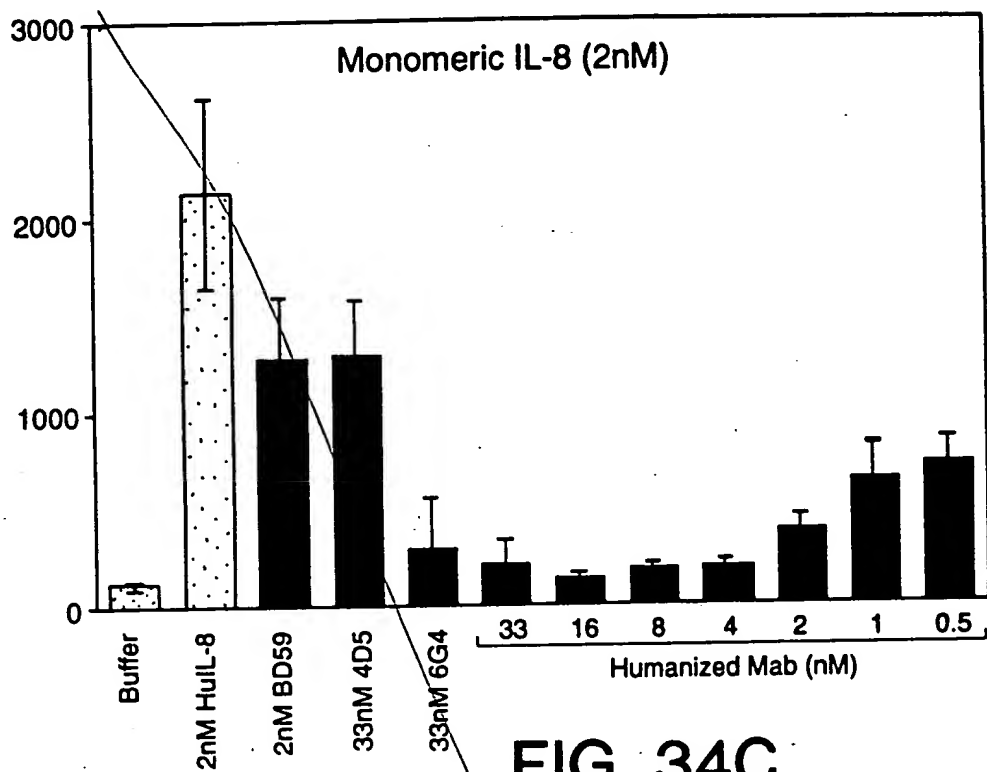


FIG. 33







**Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Light Chain**

MKKNIAFL<sup>1</sup>LLASMFVFSIATNAYADIQMTQSPSSLSASVGDRVTITCRSSQSLVHGIGATY  
LHWYQQKPGKAPKLLIYK<sup>2</sup>VS<sup>3</sup>NRFS<sup>4</sup>GVPSRFS<sup>5</sup>SGSGTDF<sup>6</sup>TLTISS<sup>7</sup>LQPEDE<sup>8</sup>FATY<sup>9</sup>CYSQST  
HVPLTFGQGTKEIKRTVAAPSVFIFPPSDEQLKSGTASV<sup>10</sup>VCLLN<sup>11</sup>NFYPPREAKVQWKVDN  
ALQSGNSQESVTEQDSKDS<sup>12</sup>TYSLSS<sup>13</sup>TLT<sup>14</sup>LSKADY<sup>15</sup>EKH<sup>16</sup>KVYACEV<sup>17</sup>THQGLSSPVT<sup>18</sup>KSFN<sup>19</sup>RG  
EC

**Amino Acid Sequence of the humanized anti-IL-8 6G4.2.5V11N35A Heavy Chain**

MKKNIAFL<sup>1</sup>LLASMFVFSIATNAYAEVQLVQSGGGLVQPGGSLRLSCAASGYSFSSHYMH  
WVRQAPGKGLEWVG<sup>2</sup>YIDPSNGET<sup>3</sup>TYNQKFKGRFTLSRDNSKNTAYLQMN<sup>4</sup>SLRAEDTAVYY  
CARGDYRYNGDWFFDVWGQGT<sup>5</sup>LVTVSSASTKGPSVF<sup>6</sup>FLAPSSKSTSGGTAALGCLVKDYF  
PEPVT<sup>7</sup>SVWN<sup>8</sup>SGALTSGVHTFPAVLQSSGLYSLSSV<sup>9</sup>TVTPSSSLGTQTYICNVN<sup>10</sup>HKPSNTK  
VDKKVEPKSCDKTHT

**Amino Acid Sequence of the putative Pepsin Cleavage Site and GCN4 Leucine Zipper**

CPPCPAPELLLGGRMKQLEDKVEELLSKNYHLENEVARLKKLVGER

**FIG. 35**

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC  
 TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG  
 -23 M K K N I A F L L A S M F V F S I A T N  
  
 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT  
 CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA  
 -3 A Y A D I Q M T Q S P S S L S A S V G D  
  
 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGCTACGTAT  
 TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACGATGCATA  
 18 R V T I T C R S S O S L V H G I G A T Y  
  
 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC  
 AATGTGACCA TAGTTGTCTT TGGTCCCTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG  
 38 L H W Y Q Q K P G K A P K L L I Y K V S  
  
 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT  
 TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA  
 58 N R F S G V P S R F S G S G S G T D F T  
  
 301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT  
 GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA  
 78 L T I S S L Q P E D F A T Y Y C S Q S T  
  
 361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA  
 GTACAGGGCG AGTGCAAACC TGTCCTCATG TTCCACCTCT AGTTTGCTTG ACACCGACGT  
 98 H V P L T F G Q G T K V E I K R T V A A  
  
 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT  
 GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA  
 118 P S V F I F P P S D E Q L K S G T A S V  
  
 481 GTGTGCCTGC TGAATAACTT CTATCCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC  
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG  
 138 V C L L N N F Y P R E A K V Q W K V D N  
  
 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC  
 CGGGAGGTTA GCCCATTGAG GGTCTCTCTA CAGTGTCTCG TCCTGTCGTT CCTGTCTGTT  
 158 A L Q S G N S Q E S V T E Q D S K D S T  
  
 601 TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC  
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG  
 178 Y S L S S T L T L S K A D Y E K H K V Y  
  
 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA  
 CGGACGCTTC AGTGGGTAGT CCCGGACTCG AGCGGGCAGT GTTTCTCGAA GTTGTCCCCT  
 198 A C E V T H Q G L S S P V T K S F N R G  
  
 721 GAGTGTTAAG CTGATCCTCT ACGCCGGACG CATCGTGGCC CTAGTACGCA ACTAGTCGTA  
 CTCACAATTC GACTAGGAGA TCGGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT  
 218 E C O

FIG. 36

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA  
 TTTTCCCATA GATCTCCAAC TCCACTAAAA TACTTTTTCT TATAGCGTAA AGAAGAACGT  
 -1 M K K N I A F L L A  
 841 TCTATGTTTCG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT  
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA  
 -11 S M F V F S I A T N A Y A E V Q L V Q S  
 901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCCGTTTGT CCTGTGCAGC TTCTGGCTAC  
 CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG  
 8 G G G L V Q P G G S L R L S C A A S G Y  
 961 TCCTTCTCGA GTCATATAT GCACTGGGTC CGTCAGGCCC CGGGTAAGGG CCTGGAATGG  
 AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTTCC GGACCTTACC  
 28 S F S S H Y M H W V R Q A P G K G L E W  
 1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT  
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA  
 48 V G Y I D P S N G E T T Y N O K F K G R  
 1081 TTCACCTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT  
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA  
 68 F T L S R D N S K N T A Y L Q M N S L R  
 1141 GCTGAGGACA CTGCCGTCTA TTACTGTGCA AGAGGGGATT ATCGCTACAA TGGTGACTGG  
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCCTAA TAGCGATGTT ACCACTGACC  
 88 A E D T A V Y Y C A R G D Y R Y N G D W  
 1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC  
 AAGAAGCTGC AGACCCCACT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG  
 108 F F D V W G Q G T L V T V S S A S T K G  
 1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG  
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC  
 128 P S V F P L A P S S K S T S G G T A A L  
 1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC  
 CCCACGGACC AGTTCCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG  
 148 G C L V K D Y F P E P V T V S W N S G A  
 1381 CTGACCAGCG GCGTGCACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTA CTCCCTC  
 GACTGGTCGC CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCCTGA GATGAGGGAG  
 168 L T S G V H T F P A V L Q S S G L Y S L  
 1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG  
 TCGTCGCACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC  
 188 S S V V T V P S S S L G T Q T Y I C N V  
 1501 AATCACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA  
 TTAGTGTTCG GGTCGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT  
 208 N H K P S N T K V D K K V E P K S C D K  
 1561 ACTCACACAT GCCCGCCGTG CCCAGCACCA GAACTGCTGG GCGGCCGCAT GAAACAGCTA  
 TGAGTGTGTA CGGGCGGCAC GGGTCGTGGT CTTGACGACC CGCCGGCGTA CTTTGTGCGAT  
 228 T H T C P P C P A P E L L G G R M K Q L

FIG. 37A

1621 GAGGACAAGG TCGAAGAGCT ACTCTCCAAG AACTACCACC TAGAGAATGA AGTGGCAAGA  
CTCCTGTTCC AGCTTCTCGA TGAGAGGTTT TTGATGGTGG ATCTCTTACT TCACCGTTCT  
248 E D K V E E L L S K N Y H L E N E V A R

1681 CTCAAAAAGC TTGTCGGGGA GCGCTAA  
GAGTTTTTCG AACAGCCCCT CGCGATT  
268 L K K L V G E R O

FIG. 37B

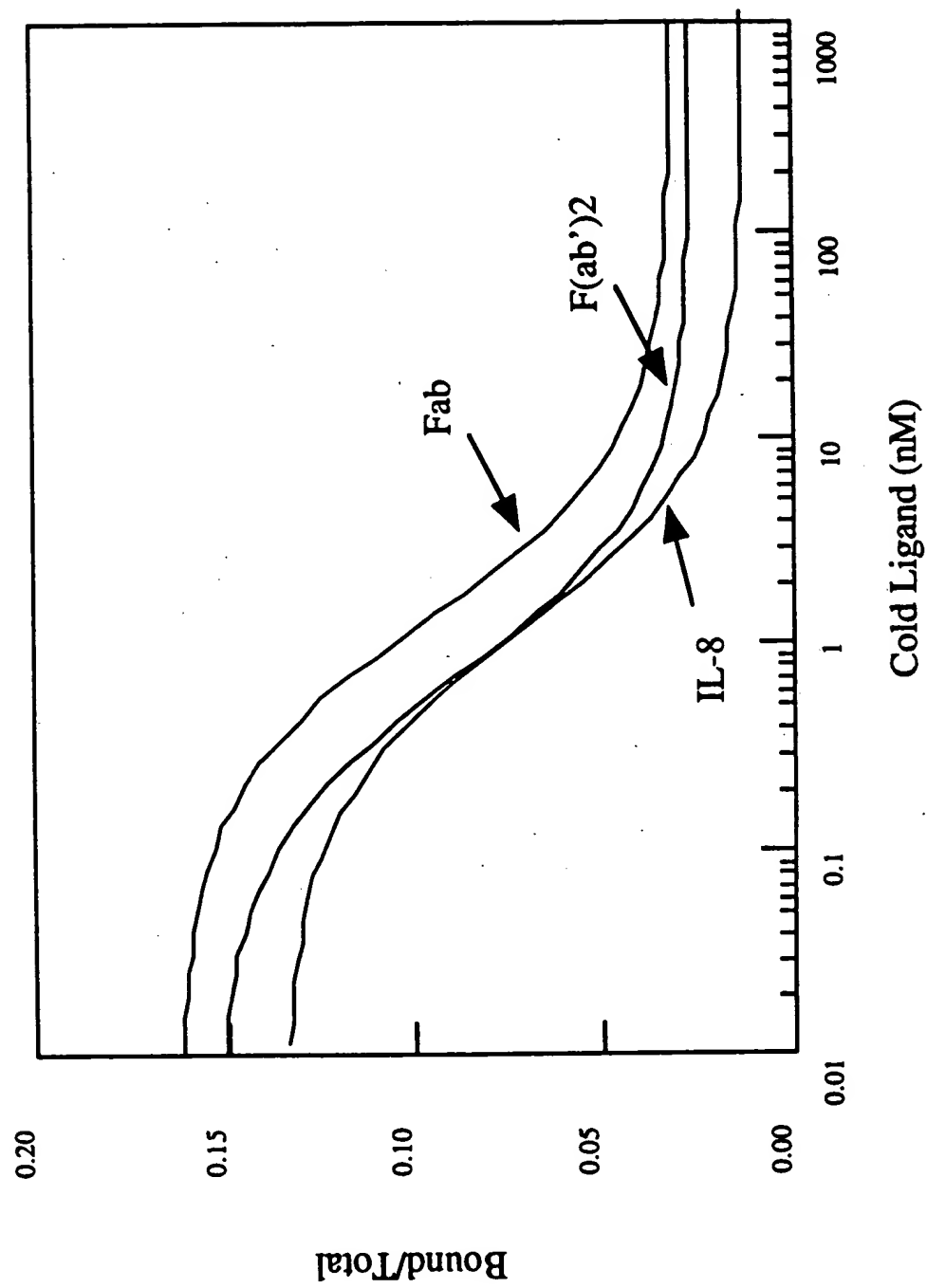
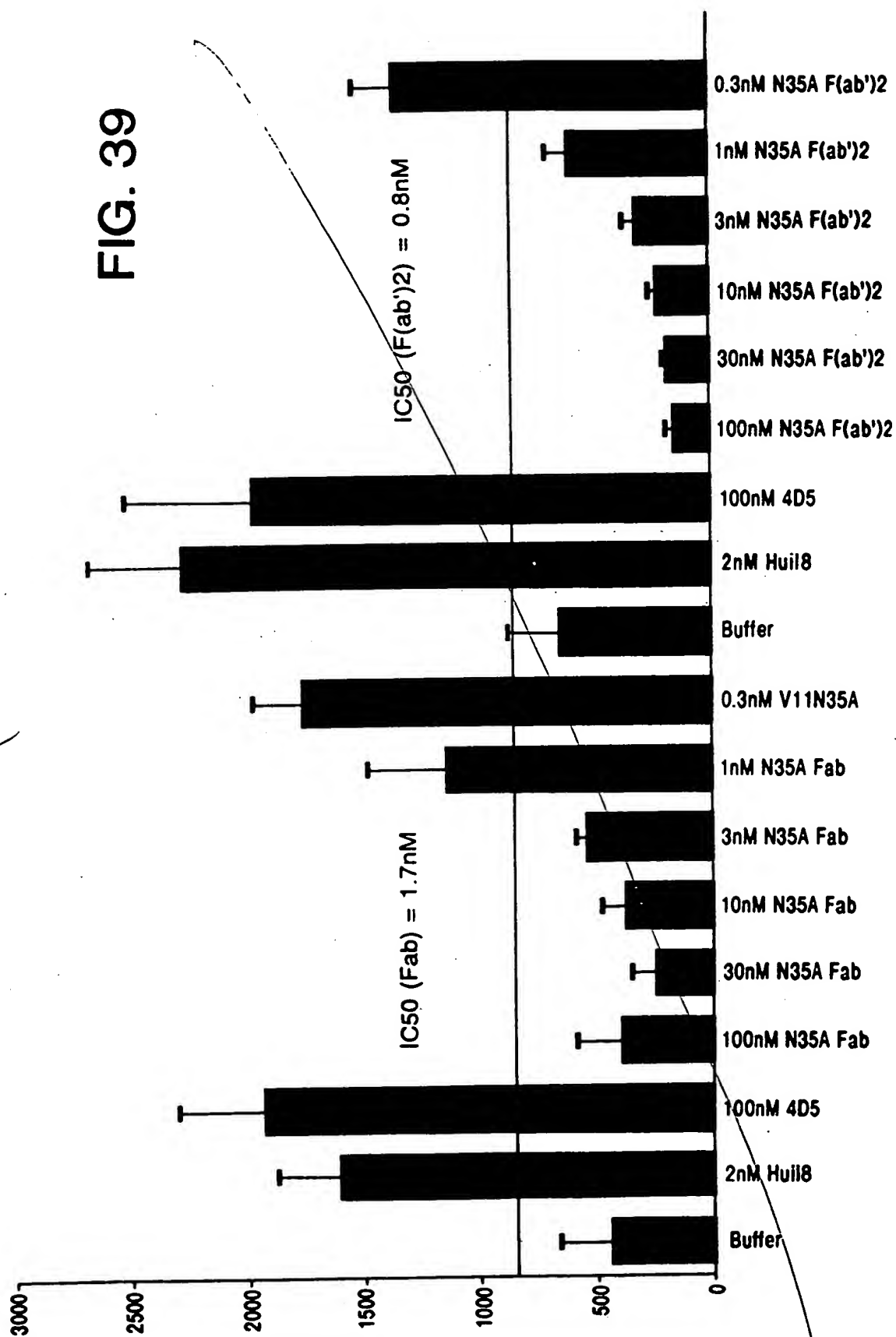


FIG. 38

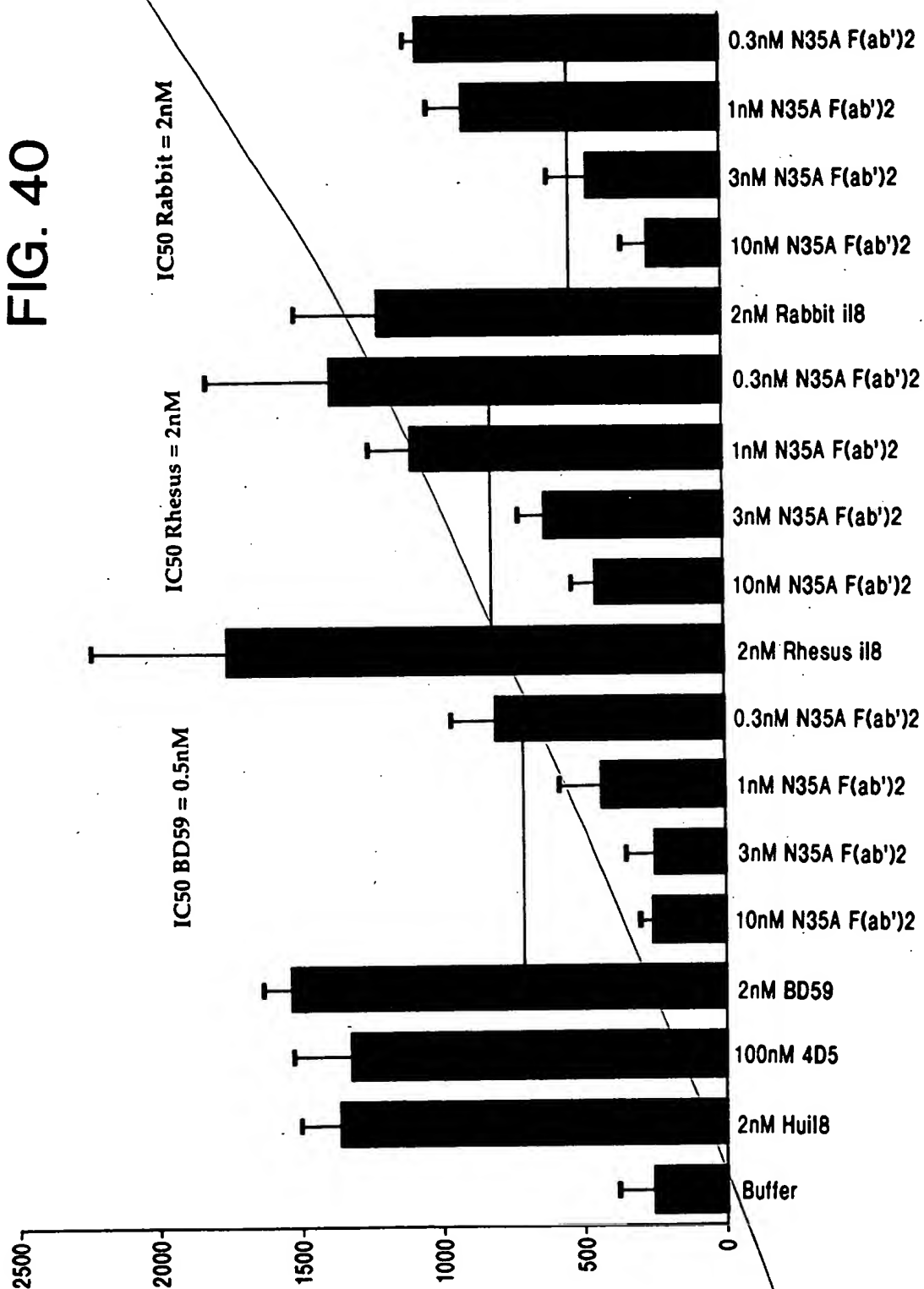
FIG. 39



Ans  
B5



FIG. 40



Ant  
Bk





```

scrFI      tfII      bsmFI
mvaI      hinfI      bsmFI
ecorII     taqI      bpmI/gsuI[dcn-]
dsav      claiI/bsp106 pleI
bstNI     bspDI[dam-] hinfI
          apyI[dcn+]
          aluI
          apyI[dcn+]
601 GGTATAGGTG CTACGTATTT ACACGTGGTAT CAACAGAAAC CAGGAAAGC TCCGAACTA CTGATTTTACA AAGTATCCAA TCGATTCTCT GGAGTCCCTT
CCATATCCAC GATGCATAA TGTGACCATA GTTGCTTTTG GTCCTTTTCG AGGCTTTGAT GACTAAATGT TTCATAGGTT AGCTAAGAGA CCTCAGGGAA
32 G I G A T Y L H W Y Q Q K P G K A P K L L I Y K V S N R F S G V P S

mspI
hpaII
bsaI
bsaWI
sau3AI
mboI/ndeII[dam-]
dpmI[dam+]
dpmII[dam-]
alwiI[dam-]
nlaIV
bstYI/xhoII
bamHI
alwiI[dam-] bsmFI
701 CTGGCTTCTC TGGATCCGGT TCTGGGACCG ATTTCACTCT GACCATCAGC AGTCTGCAGC CAGAAGACTT CGCAACTTAT TACTGTTTAC AGAGTACTCA
GAGCGAAGAG ACCTAGGCCA AGACCTGCCC TAAAGTGAGA CTGGTAGTCG TCAGACGTCG GTCTTCTGAA GCGTTGAATA ATGACAGTG TCTCATGAGT
66 R P S G S G S G T D F T L T I S S L Q P E D F A T Y Y C S Q S T H

styI
bsaJI
rsaI
csp6I
nlaIV
kpnI
hgiCI
bani
asp718
acc65I
maeII
bsrBI
aciI
bsmFI
801 TGTCCTGCTC ACCTTTGAC AGGTATCCAA GGTGGAGATC AAACGAACTG TGGCTGACC ATCTGCTTC ATCTTCCGC CATCTGATGA GCAGTTGAAA
ACAGGGCGAG TCGAAACTG TCCCATGGT CCACCTCTAG TTTGCTTGAC ACCGACGTCG TAGACAGAAG TAGAAGGCGG GTAGACTACT CGTCACTTT
99 V P L T F G Q G T K V E I K R T V A A P S V F I F P P S D E Q L K

```

FIG. 41C



[illegible]

	rsal	maei	bfai	xbaI	mnlI	hphI	mboII	sfanI		
	rsal	maei	bfai	xbaI	mnlI	hphI				
	csp6I	speI								
1201	AGTACGCAAC	TAGTCGTAA	AAGGGTATCT	AGAGTTTGAG	GTGATTTTAT	GAAAAAGAAT	ATCGCATTTTC	TTCTTGCAATC	TATGTTCCGT	TTTTCTATTG
	TCATGCGTTG	ATCAGCATTT	TTCCCATAGA	TCTCCNACTC	CACATAAATA	CTTTTCTCTTA	TAGCGTAAAG	AAGAACGTAG	ATACAAGCAA	AAAAGGATAC
						M K K N I A F L L A S M F V F S I A				

-23

```

1301 CTACAAACGC GTACGCTGAG GTTCAGCTAG TGCAGTCTGG CGGTGGCCTG GTGCAGCCAG GGGGCTCACT CCGTTTGTCC TGTGCAGCTT CTGGCTACTC
GATGTTTGGC CATGCGACTC CAAGTCGATC ACGTCAGACC GCCACCGGAC CACGTCCGTC CCCCGAGTGA GGCACAACAGG ACACGTCGAA GACCGATGAG
-5 T N A Y A E V Q L V Q S G G G L V Q P G G S L R L S C A S G Y S

```

scrFI  
ncII  
mspl  
hpall  
dsav  
cauII  
bsII  
xmal/pspAI  
smaI  
scrFI  
ncII  
dsav  
cauII  
bsII

**scrFI**  
**mvaI**  
**ecorII**

**FIG. 41E**

[illegible]

T L V T V S S A S T K G  
seq right is from p6G425chim2.fab2







2301 AATGCGCTCA TCGTCATCCT CGGCACCGTC ACCCTGGATG CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCGT CTTGCGGAT ATCGTCCATT  
TTACGGCAGT AGCAGTAGGA GCCGTGGCAG TGGGACCTAC GACATCCGTA TCCGAACCAA TACGGCCATG ACGGCCCGGA GAACGCCCTA TAGCAGGTAA

2401 CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT ATATGCGTTG ATGCAATTTC TATGGCACC CGTTCTCGGA GCACTGTCCG ACCGCTTTGG  
GGCTGTCGTA GCGTCACTG ATACCGCAGC AGCATCGCGA TATACGCAAC TAGCTTAAG ATACCGGTGG GCAAGAGCCT CGTGACAGGC TGGCGAACC

2501 CCGCGGCCCA GTCCGTGCTCG CTTGCGTACT TGGAGCCTACT ATCGACTACG CGATCATGGC GACCACACCC GTCCGTGTGA TCCTCTACGC CGGACGCATC  
GGCGGGCGGT CAGGACGAGC ACCTCGGTGA TAGTGTATGC GCTAGTACCG CTGGTGTGGG CAGGACACCT AGGAGATGCG GCCTGCGTAG

[illegible]

2901 TGGGCGGGG GCATGACTAT CGTCGCCGCA CTTATGACTG TCTTCTTTAT CATGCAACTC GTAGGACAGG TGCCGGCAGC GCTCTGGGTC ATTTTCGGCG  
 ACCGCGGCC CGTACTGATA GCAGCGCGGT GAATACTGAC AGAAGAATA GTACGTTGAG CATCCTGTCC ACGGCCGTGC CGAGACCCAG TAAAGCCGC  
 3001 AGGACCGCTT TCCTGGGAGC GGCACGATGA TCGCCTGTG GCTTGGGTA TTCGGAATCT TGCACGCCCT CGCTCAAGCC TTGCTCACTG GTCCCGCCAC  
 TCCTGGCGAA AGCGACCTCG CGCTGCTACT AGCGGACAG CGACGCCAT AAGCCTTAGA ACGTGCGGA CCGAGTTCGG AAGCAGTGAC CAGGGCGGTG  
 3101 CAAAGCTTC GGCAGAGC AGGCCATTAT CGCCGGCATG GCGCGGACG CGCTGGGCTA CGCTTGCTG GCGTTCGGA CGCGAGGCTG GATGGCCTTC  
 GTTTCGAAAG CCGCTCTTCG TCGGTGTAATA GCGCGCTGAC CCGCGGCTGC GCGACCCGAT GCAGAACGAC CGCAGCGCT CCGCTCCGAC CTACCCGGAAG

**FIG. 41K**

[illegible]

3401 GATTGTAGGC GCCGCCCTAT ACCTTGTCGT CTTCCCCGGG GTGCATGGAG CCGGGCCACC TCGACCTGAA TGGAAGCCGG CGGCACCTCG  
CTAACATCCG CGGCGGGGATA TGGAACAGAC GGAGGGGGCG AACCGACGGC CACGTACCTC GSCCCGGTGG ACCTTCGGCC GCCGTGGAGC



# Restriction

```

sau3AI
mboI/ndeII(dam-)
mamI(dam-)
dpmI(dam+)
dpmII(dam-)
bstYI/xhoII
alwI(dam-)
mspI
hpaII
mroI bsaBI(dam-)
bspMI
bspEI(dam-)
bsaMI sfanI
accIII(dam-) foki cac8I
TTATGTTCCG GATCTGCATC GCAGGATGCT GCTGGCTACC
AATACAAGGC CTAGACGTAG CGTCTACGA CGACCCGATGG
3801 TGGTCTTCGG TTTCGGTGT TCGTAAAGTC TGGAAACGGG GAAGTCAGCG CCCTGCACCA mslI
ACCAAGGCC AAGGCACAA AGCATTTTCAG ACCTTTGGC GTTCAGTCCG GGGACGTGGT
3901 CTGTGGNACA CCTACATCTG TATTAACGAA GCGCTGGCAT TGACCTGTAG TGATTTTCT CTGGTCCCG CGCATCCATA CCGCCAGTTG TTTACCCCTCA
GACACCTTGT GCATGTAGAC ATAATTGCTT CGCGACCGTA ACTGGGACTC ACTAAAAGA GACCAGGGCG GCGTAGGTAT GCGGTCAAC AAATGGGAGT
4001 CAACGTTCCA GTAACGGGC ATGTTTCATCA TCAGTAACCC GTATCGTGAG CATCCTCTCT CGTTTCATCG GTATCATTAC CCCCATGAAC AGAATTTCC
GTGCAAGGT CATTGGCCG TACAAGTAGT AGTCATTGGG CATAGCACTC GTAGGAGAGA GCAAAGTAGC CATAGTAATG GGGGTACTTG TCTTTAAGG

```

FIG. 41N







[illegible]

# Restriction Enzyme Digest

5201	TCGTGCTGAAG CCAGTTACCT TCGGAAAAG AGTTGTAGC TCTTGATCCG GCAACAAAC CACCGCTGGT AGCGTGGTT TTTTGTGTTG CAAGCAGCAG	mspi hpaII sau3AI mboI/ndeII[dam-] dpmI[dam+] dpmII[dam-] alwI[dam-] nspBII aciI cac8I fnu4HI bsoFI bbvI
	AGACGACTTC GTTCATGGA AGCCTTTTC TCAACCATCG AGAAGTAGGC CGTTGTGTTG GTGGGACCA TCGCCACCA AAAAACAAAC GTTCGTGTC	
5301	ATTACGCGCA GAAAAAGG ATCTCAAGAA GATCCTTGA TCTTTTCTAC GGGGTCTGAC GCTCAGTGA ACGAAACTC ACGTAAGG ATTTGGTCA	maeIII eco57I bsrI hinPI hhaI/cfoI thAI fndBII/mvni bstUI bsh1236I alwI[dam-] bstYI/xhoII alwI[dam-] bstYI/xhoII hgaI ddeI tru9I mseI maeII nlaIII rcal bspHI
	TAATGCGCGT CTTTTTCC TAGAGTTCTT CTAGGAACT AGAAAGATG CCCCAGACTG CGAGTCACCT TGCATTGAG TGCATTCCC TAAACCCAGT	
5401	TGAGATTATC AAAAGGATC TTCACCTAGA TCCTTTTAA TTAATAATGA AGTTTAAAT CAATCTAAG TATATAGAG TAACTTGGT CTGACAGTTA	sau3AI mboI/ndeII[dam-] rmaI hphI dpmI[dam+] mboII[dam-] sau3AI maeI tru9I mboI/ndeII[dam-] mseI dpmI[dam+] dpmII[dam-] dpmII[dam-] alwI[dam-] tru9I bstYI/xhoII bstYI/xhoII mseI alwI[dam-] bfaI ahaII/draI maeIII
	ACTCTAATAG TTTTCTAG AAGTGGATCT AGGAAATTT AATTTTACT TCAAAATTA GTTAGATTTC ATATATACTC ATTTGAACCA GACTGTCAAT	
5501	CCAATGCTTA ATCAGTGAGG CACCTATCTC AGCGATCTGT CTATTTCTGT CATCCATAGT TGCCTGACTC CCCGTCGTGT AGATAACTAC GATACGGGAG	nlaIV hgiCI banI tru9I mseI mnlI ddei dpmII[dam-] fokI pleI hinFI ahdI/eam1105I mnlI
	GGTACGAAT TAGTCACTCC GTGGATAGAG TCGCTAGACA GATAAGCAA GTAGGTATCA ACGGACTGAG GGGCAGCACA TCTATTGATG CTATGCCCTC	

FIG. 41R

[illegible]

5901

# 6001

6001 ATTCTCTTAC TGTCAATGCCA TCCGTAAGAT GCTTTTCTGT GACTGGTGAG TACTCAACCA AGTCATTCTG AGRATAGTGT ATGCGGCGAC CGAGTTGCTC  
 TAAGAGATG ACAGTACGCT AGGCATTCTA CGAAAGACA CTGACCACTC ATGAGTTGGT TCAGTAAGAC TCTATACACA TACGCGCGTG GCTCAACGAG

6101 TTGCCCCGGC TCAACACGGG ATATATCCGC GCCACATAGC AGAAGTTTAA AAGTGCTCAT CATTGGHAAA CGTTCTTCGG GCGGAAAACT CTCAGGATC  
 AACGGGCGC AGTTGTGCC TATTATGGC GGTGTATCG TCTTGAATT TTCACGAGTA GTAACCTTTT GCAAGAAGCC CCGCTTTTGA GAGTTCTCTAG

6201 TTACCGCTGT TGAGATCCAG TTCGATGTAA CCCACTCGTG CACCCAACTG ATCTTCAGCA TCTTTTACTT TCACCAGCGT TTCTGGGTGA GCAAAAACAG  
 AATGGCGACA ACTCTAGTGC AAGCTACATT GGTGAGCAC GTGGGTGAC TAGAAGTCGT AGAAAATGAA AGTGGTGGCA AGACCCACT CGTTTTTGTC

6301 GAAGGCAAAA TGCCGCAAAA AAGGGAATAA GGGCGACACG GAAATGTTGA ATACTCATAC TCTTCTTTT TCAATATAT TGAAGCATTT ATCAGGTTA  
 CTTCGGTTTT ACGCGTTTT TTCCCTTATT CCCGCTGTGC CTTTACAATG TAGAGTATG AGAAGGAAAA AGTTATAATA ACTTCGTAAA TAGTCCCAAT

FIG. 41T

6401	<p> nlaIII  rcal  bspHI  bsrBI  bsmAI  TGGTCTCATG  ACCGGATACA  TATTTGAATG  TATTTAGAAA  AATAAACAAA  TAGGGTTCC  GGCACATTT  CCCCGAAAAG  TGCACCTGA  CGTCTAAGAA  aaiI  aatII  dclI  maeII  hinII/acyI  ahaII/bsaHI  bstUI  bshI236I  fndI/mvni  thai  hinPI </p>	<p> nlaIV  hhaI/cfoI  ATCCTGTTT  ATCCCAAGG  CGCGTGTAA  GGGCTTTTC  ACGCTGGACT  GCAGATTCTT </p>
6501	<p> nlaIII  rcal  bspHI  mseI  tru9I  bssI  bssI  bpuAI  mboII  sau96I  haeIII/palI  asuI  ecoO109I/draII  mnlI  nlaIII  rcal  bspHI  mseI  tru9I </p>	<p> bssI  bssI  bpuAI  mboII  sau96I  haeIII/palI  asuI  ecoO109I/draII  mnlI  nlaIII  rcal  bspHI  mseI  tru9I </p>

**FIG. 41U**

```

>length: 6563

aatII(GACGTC):      1645 6489
acc65I(GGTACC):      403 823
accI(GTHKAC):      1093 1963 4449
accIII(TCCGGA):      3867(dam-)
aciI(CCGC):      178 542 805 877 1340 1750 1826 2011 2039 2043 2182 2242 2384 2492 2501 2504
                2628 2781 2784 2787 2906 2926 3005 3045 3094 3141 3226 3241 3309 3342 3367 3412
                3436 3448 3490 3544 3597 3613 3619 3700 3838 3967 3970 3981 4139 4155 4210 4266
                4351 4390 4400 4442 4467 4505 4518 4544 4561 4604 4611 4632 4723 4751 4878 4897
                5018 5128 5263 5272 5634 5725 5916 5962 6083 6127 6204 6313 6412 6459
acyI      see hiniI
aflIII(ACRYGT):      1307 4678
ageI(ACCGT):      1788
ahaII(bsaHI(GRCGYC):      1645 1813 2616 2637 2751 3408 6107 6489
ahaII(draI(TTTAA):      5435 5454 6146
ahdI/eam1105I(GACNNNNGTC):      346 5566
alulI(AGCT):      72 121 252 320 398 532 589 648 1126 1144 1167 1325 1386 1906 2054 2075 2126
                2218 2233 2889 3292 4202 4259 4270 4319 4338 4619 4845 4935 4981 5238 5759 5859
                5922
alw44I/snoI(GTGCAC):      1831 4494 4992 6238
alwI(dam-)(GGATC):      412 413 712 713 1171 1471 2578 2579 3300 3870 5245 5319 5331 5416 5429 5893
                6196 6214
alwNI(dcm-)(CAGNNNCTG):      1117 1385 5089
apaI(GGGCCC):      1695
apaLI/snoI(GTGCAC):      1831 4494 4992 6238
apoI(RAATTY):      1 391 4093
apyI(dcm+)(CCWGG):      640 999 1347 1357 1449 1665 1713 1755 1764 2333 3262 3645 4705 4826 4839
aseI/asni/vspI(ATTAAAT):      5742
asni      see aseI
asp700(GAANNNTTC):      905 930 4234 6166
asp718(GGTACC):      403 823
aspHI      see hgiAI
aspi      see thl11I
asuI(GGNCC):      1119 1195 1425 1434 1446 1512 1695 1696 1752 2155 2375 2727 3002 3090 3339 3463

```

FIG. 41V

Stop-Template Primer

SL.97.2      5' CAT GGT ATA GGT TAA ACT TAT TTA CAC 3'

NNS Randomization Primer

SL.97.3      5' CAT GGT ATA GGT NNS ACT TAT TTA CAC 3'

FIG. 42



# Randomization of Position N35 of Variable Light Chain CDR-1 Amino Acid Frequency

## *Phage Display (NNS Codon Library) Sort #3*

Amino Acid	Frequency	% Total	IC50 (nM)
Asparagine (wt)	1	5.6	4.9
Glycine	6	16.6	3.1
Aspartic Acid	3	16.6	3.1
Glutamic Acid	4	22.2	0.1
Alanine	2	5.6	0.2
Lysine	1	5.6	ND
Serine	1	1.9	ND

FIG. 43A

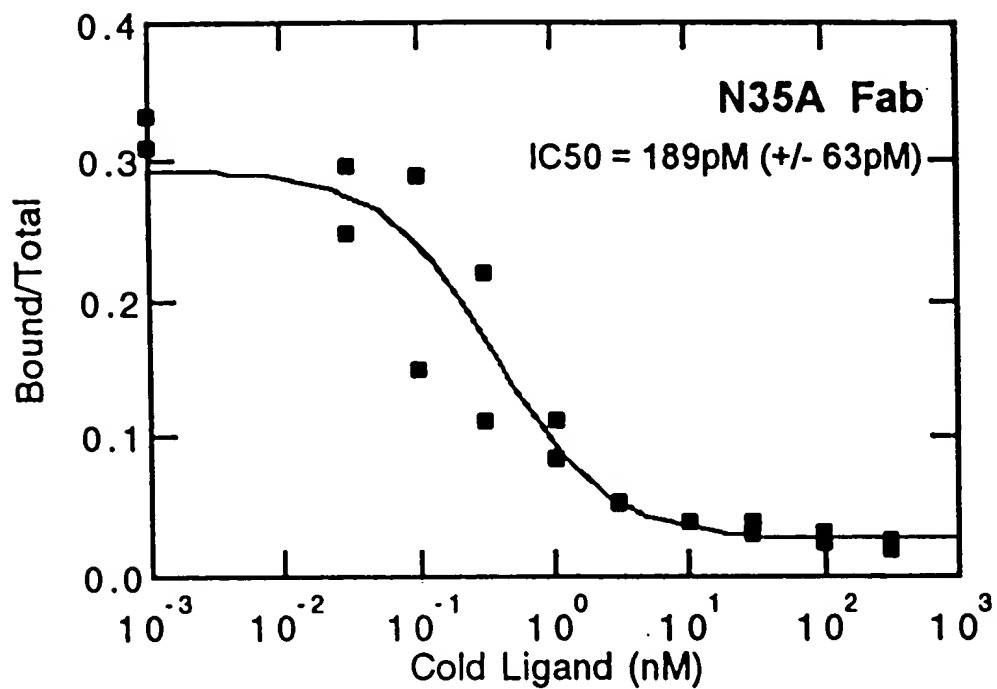


FIG. 43B-1

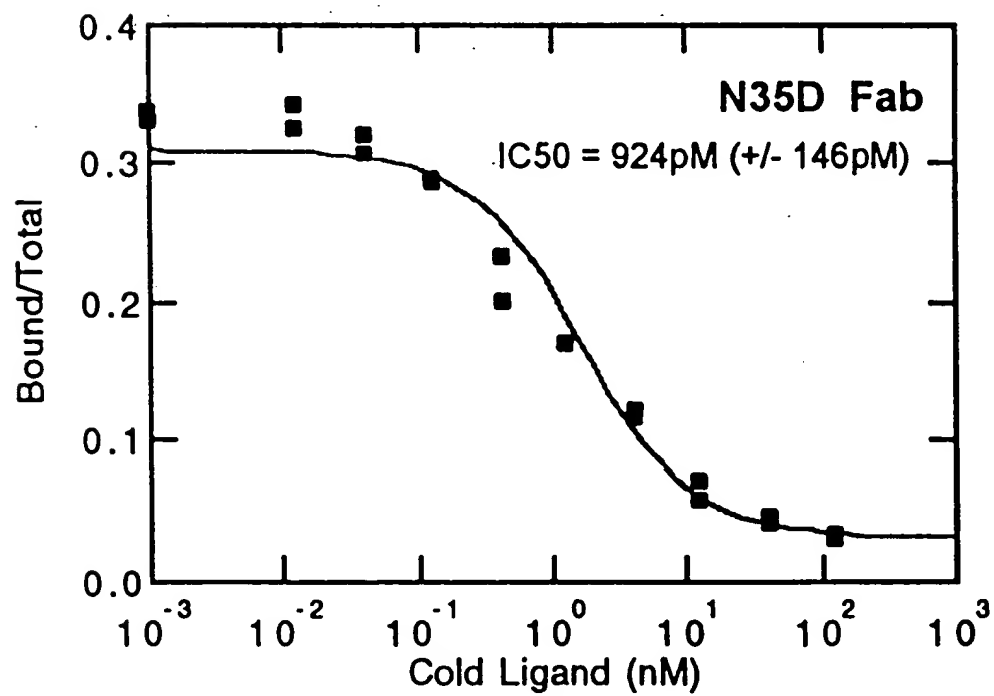


FIG. 43B-2

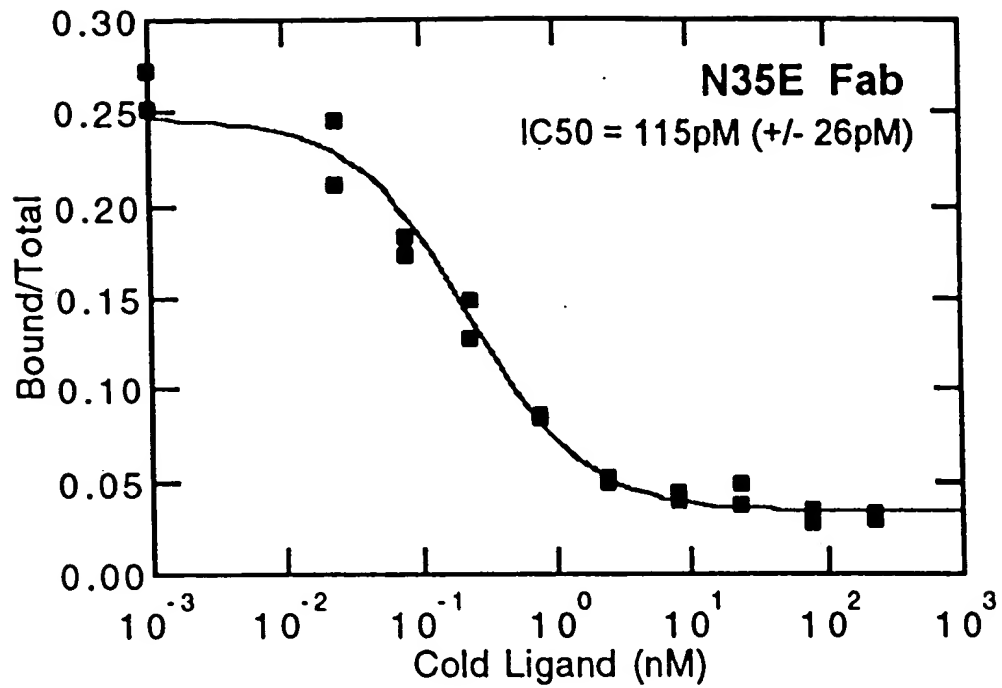


FIG. 43B-3

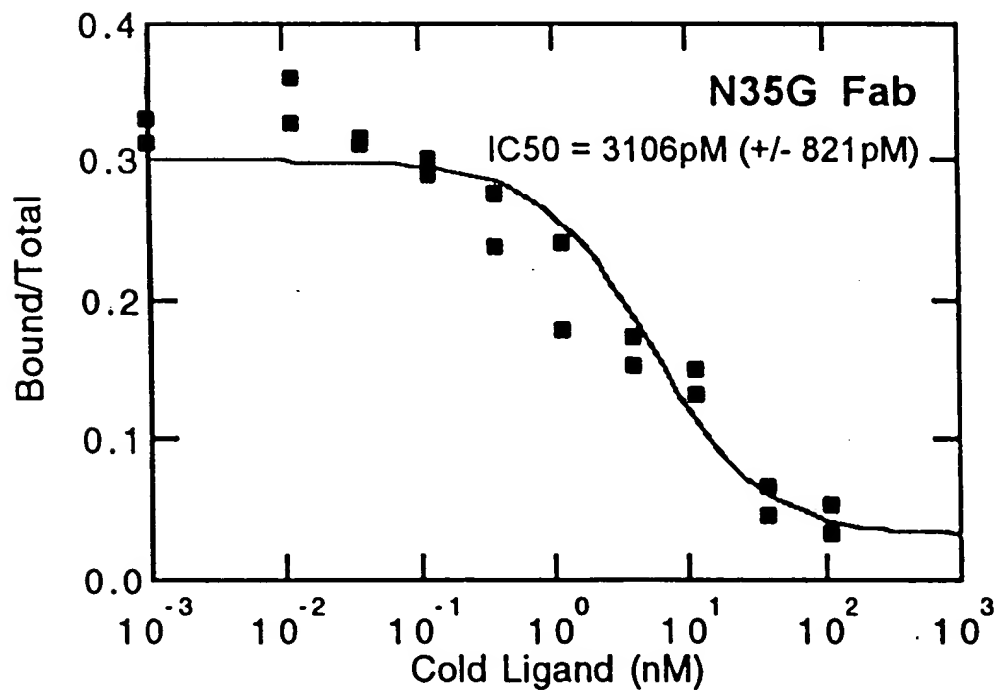


FIG. 43B-4

A line graph showing the concentration of Fab (molar) on the y-axis versus time in seconds on the x-axis. The y-axis ranges from 0 to 8E-10 with major ticks every 1E-10. The x-axis ranges from 0 to 10,000 seconds with major ticks every 1,000 seconds. Data points are marked with 'X' and connected by a smooth curve. The concentration starts at approximately 7.5E-10 at 0 seconds, remains relatively constant until about 1,000 seconds, then increases sharply, reaching a plateau of approximately 2.0E-10 by 6,000 seconds.

Time (Seconds)	Fab (molar)
0	7.5E-10
1000	4.0E-10
2000	2.5E-10
3000	2.2E-10
4000	2.1E-10
5000	2.0E-10
6000	2.0E-10

**Representative Conc versus Time Plot. Shown is the kinetic data for 6G4V11N35A.F(ab')<sub>2</sub>.**

SAMPLE	k <sub>a</sub>	k <sub>d</sub>	K <sub>d</sub>
6G4V11N35A-Fab	ND	ND	114pM
6G4V11N35A-F(ab') <sub>2</sub>	2.0x10 <sup>6</sup>	2.1x10 <sup>-4</sup>	109pM
6G4V11N35E-Fab	4.7x10 <sup>6</sup>	2.6x10 <sup>-4</sup>	54pM

FIG. 44

1 ATGAAAAAGA ATATCGCATT TCTTCTTGCA TCTATGTTTCG TTTTCTCTAT TGCTACAAAC  
 TACTTTTTCT TATAGCGTAA AGAAGAACGT AGATACAAGC AAAAAAGATA ACGATGTTTG  
 -23 M K K N I A F L L A S M F V F S I A T N  
 61 GCATACGCTG ATATCCAGAT GACCCAGTCC CCGAGCTCCC TGTCCGCCTC TGTGGGCGAT  
 CGTATGCGAC TATAGGTCTA CTGGGTCAGG GGCTCGAGGG ACAGGCGGAG ACACCCGCTA  
 -3 A Y A D I Q M T Q S P S S L S A S V G D  
 121 AGGGTCACCA TCACCTGCAG GTCAAGTCAA AGCTTAGTAC ATGGTATAGG TGAGACGTAT  
 TCCCAGTGGT AGTGGACGTC CAGTTCAGTT TCGAATCATG TACCATATCC ACTCTGCATA  
 18 R V T I T C R S S O S L V H G I G E T Y  
 181 TTACACTGGT ATCAACAGAA ACCAGGAAAA GCTCCGAAAC TACTGATTTA CAAAGTATCC  
 AATGTGACCA TAGTTGTCTT TGGTCCTTTT CGAGGCTTTG ATGACTAAAT GTTTCATAGG  
 38 L H W Y Q Q K P G K A P K L L I Y K V S  
 241 AATCGATTCT CTGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC GGATTTCACT  
 TTAGCTAAGA GACCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG CCTAAAGTGA  
 58 N R F S G V P S R F S G S G S G T D F T  
 301 CTGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTTC ACAGAGTACT  
 GACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAAG TGTCTCATGA  
 78 L T I S S L Q P E D F A T Y Y C S O S T  
 361 CATGTCCCGC TCACGTTTGG ACAGGGTACC AAGGTGGAGA TCAAACGAAC TGTGGCTGCA  
 GTACAGGGCG AGTGCAAACC TGTCCCATGG TTCCACCTCT AGTTTGCTTG ACACCGACGT  
 98 H V P L T F G Q G T K V E I K R T V A A  
 421 CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT  
 GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TTAGACCTTG ACGAAGACAA  
 118 P S V F I F P P S D E Q L K S G T A S V  
 481 GTGTGCCTGC TGAATAACTT CTATCCAGA GAGGCCAAAG TACAGTGGAA GGTGGATAAC  
 CACACGGACG ACTTATTGAA GATAGGGTCT CTCCGGTTTC ATGTCACCTT CCACCTATTG  
 138 V C L L N N F Y P R E A K V Q W K V D N  
 541 GCCCTCCAAT CGGGTAACTC CCAGGAGAGT GTCACAGAGC AGGACAGCAA GGACAGCACC  
 CGGGAGGTTA GCCCATTGAG GGTCTCTCA CAGTGTCTCG TCCTGTGCTT CCTGTCTGTTG  
 158 A L Q S G N S Q E S V T E Q D S K D S T  
 601 TACAGCCTCA GCAGCACCTT GACGCTGAGC AAAGCAGACT ACGAGAAACA CAAAGTCTAC  
 ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCTGCTGA TGCTCTTTGT GTTTCAGATG  
 178 Y S L S S T L T L S K A D Y E K H K V Y  
 661 GCCTGCGAAG TCACCCATCA GGGCCTGAGC TCGCCCGTCA CAAAGAGCTT CAACAGGGGA  
 CGGACGCTTC AGTGGGTAGT CCCGGAAGTC AGCGGGCAGT GTTTCTCGAA GTTGTCCCCT  
 198 A C E V T H Q G L S S P V T K S F N R G  
 721 GAGTGTTAAG CTGATCCTCT ACGCCGAGC CATCGTGGCC CTAGTACGCA ACTAGTCGTA  
 CTCACAATTC GACTAGGAGA TGCGGCCTGC GTAGCACCGG GATCATGCGT TGATCAGCAT  
 218 E C O

FIG. 45

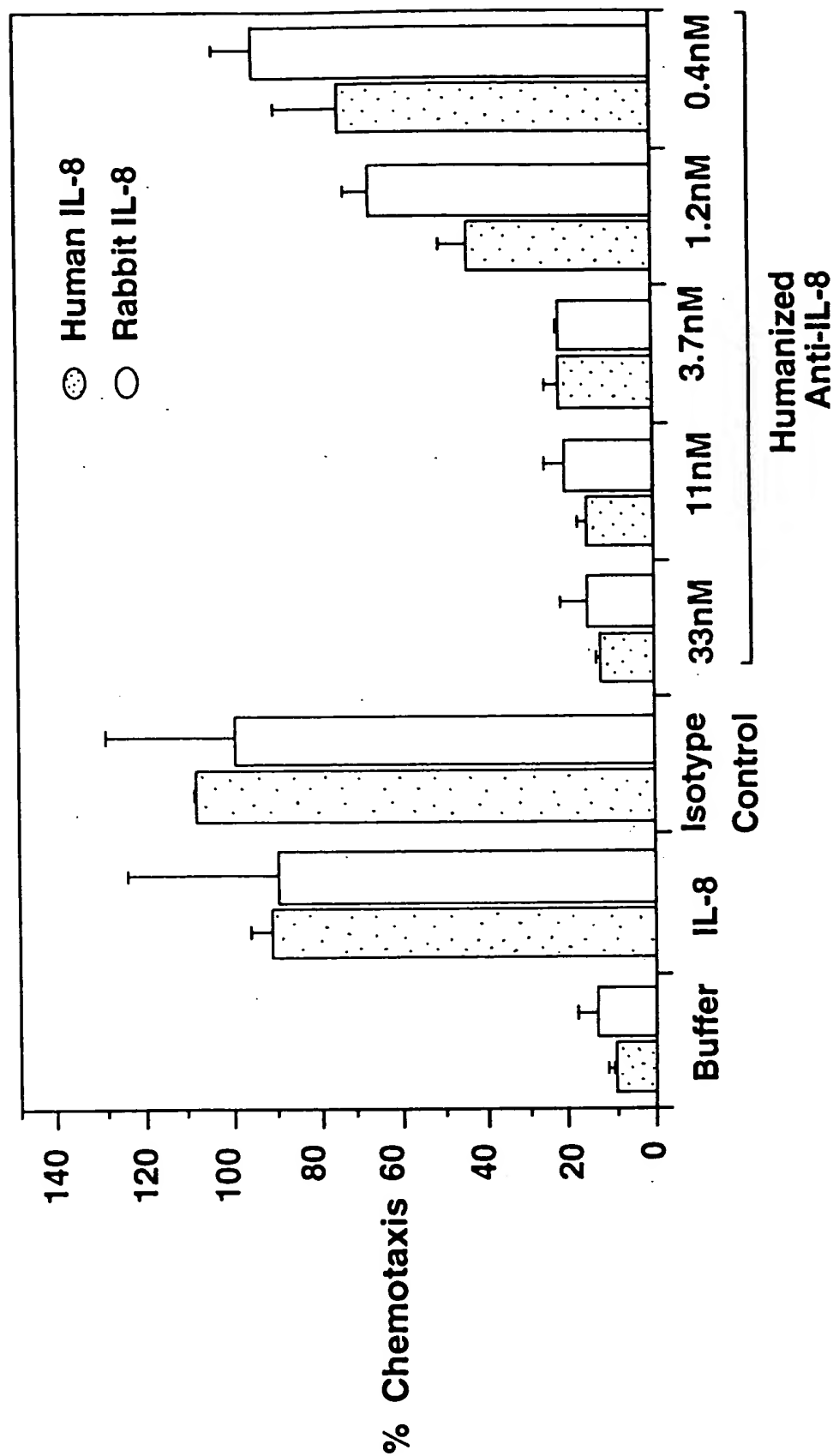


FIG. 46

N35AH1upr

5'-CTAGTGCAGTCTGGCGGTGCCCTGGTGCAGCCAGGGGGCTCACTCCGTTTGTCCTGTGCAGCTTCTGGCTACTCCTTC-3'

N35AH1lwr

5'-TCGAGAAGGAGTAGCCAGAAAGCTGCACAGGACAAACGGAGTGAGCCCCCTGGCTGCACCAGGCCACGCCAGACTGCACT  
AG-3'

Bold indicates nucleotide change destroying PvuII site.

FIG. 47

```

> Wed May 7 18:27:36 1997
> /home/ruby/vc/Immbio/afan/ss.p6G425v11.N35A.choSD
> sites: std
> length: 8120 (circular)
> This has the pSVI backbone with the pRK7 cloning linker (pSVI7) and the intron DHFR(ID)
> made from pSVI.WTSD.D by adding a linearization linker(LL) into the HpaI site

```

```

cac8I
alul
sstI
sacI
hgiJII
hgiAI/aspHI
ec1136II
bsp1286
bsiHKAI
bmyI
banII
taqI
1 TTGAGCTCG CCCGACATTTG ATTATTGACT AGAGTCGATC GACAGCTGTG GAATGTGTGT CAGTTAGGGT GTGGAAGTC CCCAGGCTCC CCAGCAGGCA
AAGCTGAGC GGGCTGTAAC TAATAACTGA TCTCAGCTAG CTGTGCACAC CTTACACACA GTCAATCCCA CACCTTTTCAG GGTCCGAGG GTCGTCCGT
scrFI mvaI ecorII dsav bstNI apyI(dcm+) bsaJI bsmFI nlaIV cac8I
sau3AI alul mboI/ndeII(dam-) dpnI(dam+) pvuI/bspCI pleI dpnII(dam-) hinfI taqI(dam-) rmaI mcrI pvuII bsaJI nsp8II
maeI bfaI taqI(dam-)
sfanI ppulOI nsiI/avaIII nlaIII sphi nspI nspHI cac8I
scrFI mvaI ecorII dsav bstNI apyI(dcm+) bsaJI bsmFI nlaIV cac8I
sexAI
101 GAAGTATGCA AAGCATGCCAT CTCAATTAGT CAGCAACCAG GTGTGGAAG GTCCCAAGGT CCCACGAGG CAGNAGTATG CAAAGCATGC ATCTCAATTA
CTTCATACGT TTGCTACGTA GAGTTAATCA GTCGTTGGTC CACACCTTC AGGGTCCGA GGGGTCTGTC GTCTTCATAC GTTTCGTACG TAGAGTTAAT
nlaIII styI ncoI bsiI deaI aciI bsaJI
201 GTCAGCAACC ATAGTCCCGC CCCTAACTCC GCCATCCCG CCCCTAACTC CGCCAGTTC CGCCCATTC TCT CGCCCATG GCTGACTAAT TTTTATTAT
CAGTCGTTGG TATCAGGGCG GGGATTGAG GGGATTGAG GCGGTTCAAG GCGGTTAAGA GCGGGGTAC CGACTGATTA AAAAATAA

```

FIG. 48A



FIG. 48B

# Restriction Enzyme Sites

601 CAAAGAATGA CCACAACTTC TTCAGTGGAA GGTAACAGA ATCTGGTGAT TATGGGTAGG AAAACCTGGT TCTCCATTCC TGAGAAGAAT CGACCTTTAA  
 GTTCTTACT GGTGTGGAG AAGTCACCTT CCATTGTCT TAGACCACCTA ATACCCTCC TTTGGACCA AGAGGTAAGG ACTCTTCTTA GCTGGAAT  
 Restriction Enzymes:   
 eco57I mboII earI/ksp632I mnlI tfII hinfI hphI alwNI(dcm-) sexAI ddeI mboII taqI ehaII/draI  
 scrFI mvaI ecorII dsav bstNI apyI(dcm+) tru9I mseI  
 sstI sacI hgiII hgiAI/aspHI ecl136II bsp1286 bsiHKA I bmyI  
 701 AGGACAGAAT TAATATAGT CTCAGTAGAG AACTCAAGA ACCACCACGA GGAGCTCAT TTCTTGCCAA AAGTTTGGAT GATGCCTTAA GACTTATTGA  
 TCCTGTCTTA ATTATATCAA GATCATCTC TTGAGTTCT TGGTGGTGCT CCTCGAGTAA AAGAAGGTT TCAAAACCTA CTACGGAAT CTGAATAACT  
 Restriction Enzymes:   
 tru9I mseI aaeI/asnI/vspI ddeI mnlI aluI mnlI aluI bssI banII bali bseRI bstXI foki sfaNI mseI  
 aflII/bfrI  
 801 ACAACCGGAA TTGGCAAGTA AAGTAGACAT GGTGTGGATA GTCCGAGGCA GTTCTGTTTA CCAGGAAGCC ATGAATCAAC CAGGCCACCT TAGACTCTTT  
 TGTGGCCTT AACCGTTCAT TTCACTCTGA CCAAACCTAT CAGCTCCGT CAAGACAAAT GGTCTTCGG TACTTAGTGT GTCCGGTGA ATCTGAGAA  
 Restriction Enzymes:   
 mspI hpaII bsaWI accI nlaIII mnlI bstNI ddeI pleI  
 scrFI mvaI ecorII dsav tfII dsav apyI(dcm+) hinfI apyI(dcm+) hinfI  
 haeIII/palI haeI

FIG. 48C

CTGAGTTCCT AGTACGTCCT TAACTTTTCA CTGTGCAAAA AGGCTCTTTA ACTAAACCCC TTATATATTG GAGAGGGTCT TATGGGTCCG CAGGAGAGAC

901 GTGACAAGGA TCATGCAGGA ATTGAAAGT GACACGTTTT TCCAGAAAT TGATTTGGGG AATATATAAC CTCTCCAGA ATACCCAGGC GTCCTCTCTG  
 CACTGTCCT AGTACGTCCT TAACTTTTCA CTGTGCAAAA AGGCTCTTTA ACTAAACCCC TTATATATTG GAGAGGGTCT TATGGGTCCG CAGGAGAGAC

scrFI  
 mvaI  
 ecorII  
 dsav  
 bstNI  
 apyI(dcm+)  
 sau96I

1001 AGGTCCAGGA GGAAGAGGC ATCAAGTATA AGTTTGAAGT CTACGAGAAG AAAGACTAAC AGAAGATGC TTTCAAGTTC TCTGCTCCCC TCCTAAAGCT  
 TCCAGGTCCT CTTTTTCCG TAGTTCATAT TCRAACTCA GATGCTCTTC TTCTGATTG TCCTTCTACG AAAGTTCAAG AGAGGAGGG AGGATTTCGA

styI  
 bsaJI

sau3AI  
 mboI/ndeII(dam-)  
 dpnI(dam+)  
 dpnII(dam-)  
 alwI(dam-)  
 bstYI/xhoII

ppu10I  
 nsiI/avaII  
 nlaIII  
 styI  
 ncoI  
 dsai bsmFI  
 bsaJI  
 cac8I

1101 ATGCATTTT ATAAGACCAT GGCACTTTGG CTGGCTTTAG ATCCCTTGG CTTCGTTAGA ACCGAGCTAC AATTAATACA TAACTTTATG TATCATAAC  
 TACGTAAAA TATTCGTGTA CCTGAAAAAC GACCGAATC TAGGGGAACC GAAGCAATCT TCGCTCGATG TTAATTATGT ATTGGAATAC ATAGTATGTG

sau96I  
 avall  
 asuI  
 scrFI  
 mvaI  
 ecorII

FIG. 48D

1201 ATACGATTAA GGTGACACTA TAGATACAT CCACCTTGCC TTCTCTCCA CAGGTGTCCA CTCCACGTC CAACGTCACC TCGGTTCTAT CGATTGAATT  
TATGCTAAAT CCACTCTGAT ATCTATTGTA GGTGAAACGG AAAGAGAGGT GTCCACAGGT GAGGGTCCAG GTTACAGTGG AGCCAAGATA GCTRACTTAA  
seq from PRK6G425VH: Cla-AvrII^

1301 CCACATGGG ATGGTCATGT ATCATCCTTT TTCTAGTAGC AACTGCAACT GGAGTACATT CAGAAGTTCA GCTAGTGCAG TCTGGCGGTG GCCTGGTGCA  
GGTGTACCC TACCAGTACA TAGTAGGAAA AAGATCATCG TTGACGTTGA CCTCATGTAA GTCTTCAAGT CGATCAGTC AGACGCCAC CGGACCCAGT  
E V Q L V Q S G G L V Q

1

1401 GCCAGGGGC TCACCTCCGTT TGTCCTGTGC AGCTTCTGCG TACTCCTTCT CGAGTCACTA TATGCACTGG GTCCGTCAGG CCCCGGGTAA GGGCCTGGAA  
CGGTCCCCCG AGTGAGGCA ACAGGACAGG TCGAAGACCG ATGAGGACCG GTCTAGTGA GCTCACTGAT ATACGTGACC CAGGCAGTCC GGGGCCCAT CCCTGACCTT  
14 P G S L R L S C A A S G Y S F S S H Y M H W V R Q A P G K G L E

FIG. 48E

bslI  
 sau3AI  
 mboI/ndelI[dam-]  
 dpmI[dam+]  
 dpmII[dam-]  
 alwI[dam-] hphI  
 1501 TGGGTTGGAT ATATTGATCC TTCCAATGGT GAACACTACGT ATAATCAAAA GTTCACGGG CGTTTCACIT TATCTCGCGA CAACTCCAAA AACACAGCAT  
 ACCCAACCTA TATAACTAGG AAGGTACCA CTTTGATGCA TATTAGTTT CAAGTTCCCG GCAAAGTGAA ATAGAGCGT GTTGAGGTTT TTGTGTGCTA  
 47 W V G Y I D P S N G E T T Y N Q K F K G R F T L S R D N S K N T A Y  
  
 scfI  
 pstI  
 bsgI  
 bspMI  
 1601 ACCTGCAGAT GAACAGCCTG CGTGTGAGG ACACCTGCGT CTATTACTGT GCAAGAGGGG ATTATCGCTA CAATGGTGAC TGGTCTTTCG ACGTCTGGGG  
 TGGACGTCTA CTTGTGGGAC GCACGACTCC TGTGACGGCA GATAATGACA CGTTCTCCCG TAATAGCGAT GTTACCACCTG ACCAAGAAGC TGCAGACCCC  
 81 L Q M N S L R A E D T A V Y Y C A R G D Y R Y N G D W F F D V W G  
  
 hinII/acyI  
 ahaII/bsaHI  
 aatII  
 bsrI  
 maeIII  
 hphI  
 mboII maeII  
 taqI  
 1701 TCAAGGAACC CTGCTCACC GTCTCTCGG CTTCCACCAAG GGCCCATCGG TCTTCCCGCT GGCACCTCC TCCAAGAGCA CCTCTGGGGG CACAGCGGCC  
 AGTTCCTTGG GACCACTGGC AGAGGAGCGG GAGGTGGTTC CCGGGTAGCC AGAAGGGGGA CCGTGGGAGG AGGTCTCGT GGAGACCCCG GTGTGCGCCG  
 114 Q G T L V T V S S A S T K G P S V F P L A P S S K S T S G G T A A  
  
 scrFI  
 mvaI  
 ecorII  
 dsav  
 bstNI  
 bsaJI  
 sau96I  
 haeIII/palI  
 asuI  
 fnu4HI  
 bsoFI  
 bsp1286 aciI bsaJI  
 bmyI nspBII apyI[dcM+]

FIG. 48F

scrFI  
 mvaI  
 ecorII  
 econI  
 dsav  
 bstNI  
 bali  
 apyI[dcn+]  
 fnu4HI  
 bsoFI  
 bvi  
 1801 CTGGGCTGCC TGGTCAAGGA CTACTTCCCG GAACTCAGG CGGTGCTGTG GAACTCAGG CCGCTGACCA CGCGGTGCA CACCTTCCCG GCTGTCTCTAC  
 GACCCGACGG ACCAGTTCCT GATGAAGGG CTTGGCCACT GCCACAGCAC CTTGAGTCCG CGGGACTGCT CGCGCACGT GTGGAAGGCG CGACAGGATG  
 147 L G C L V K D Y F P E P V T V S W N S G A L T S G V H T F P A V L Q

fnu4HI  
 bsoFI  
 nlaIV  
 hgiCI  
 bni  
 bsp1286  
 maeIII  
 hphI  
 bmyI  
 bvi  
 1901 AGTCCCTCAG ACTTACTCC CTCAGCAGCG TGGTCACTGT GCCCTCTAGC AGCTTGGGCA CCCAGACCTA CATCTGCAAC GTGAATCACA AGCCAGCACA  
 TCAGGAGTCC TGAGATGAGG GAGTCTGCGC ACCACTGACA CGGGAGATCG TCGAACCCGT GGTCTGAT GTAGACGTTG CACTTAGTGT TCGGTCTGTT  
 181 S S G L Y S L S S V V T V P S S S L G T Q T Y I C N V N H K P S N

hgiAI/aspHI  
 bsp1286  
 bsiHKA  
 bmyI  
 cac8I  
 fnu4HI  
 bsoFI  
 acII  
 apaLI/enoI  
 dsav  
 scfI  
 alw4I/enoI  
 cauII  
 2001 CACCAAGGTG GACAAGAAAG TTGAGCCCAA ATCTTGTGAC AAAACTCACA CATGCCACCC GTGCCCGACA CCTGAACCTCC TGGGGGGACC GTCACTCTTC  
 GTGGTTCCAC CTGTTCTTTC AACTCGGGT TAGAACACTG TTTGAGTGT GTACGGGTGG CACGGGTCTG GGACTTGAGG ACCCCCTGG CAGTCAGAAG  
 214 T K V D K K V E P K S C D K T H T C P P C P A P E L L G G P S V F

FIG. 48G



2401 CAGCCCCGAG AACACAGGT GTACACCCCTG CCCCACATCCC GGAAGAGAGAT GACCAAGAAC CAGGTCAGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA

scrFI  
ncII  
mapi  
hpaII  
dsav  
cauII  
xmaI/pspAI  
smaI  
scrFI  
ncII  
dsav  
cauII

scrFI mvaI  
ecorII  
dsav  
bstNI  
apyI(dcm+)  
sexAI  
bspMI  
apyI(dcm+)

2401 CAGCCCCGAG AACACAGGT GTACACCCCTG CCCCACATCCC GGAAGAGAGAT GACCAAGAAC CAGGTCAGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA  
347 Q P R E P Q V Y T L P P S R E E M T K N Q V S L T C L V K G F Y P S

mspi  
hpaII

fnu4HI  
bsoFI  
bbvI

pleI  
hinfi  
nlaIV mboII scfI cac8I

msli bsaJI

bsrDI

bsvI

mnII

mnII

pleI

mnII

2501 GCGACATCGC CGTGGAGTGG GAGAGCAATG GGCAGCCCGA GAACAACTAC AAGACCAACG CTCCGCTGCT GGACTCCGAC GGCTCCTTCT TCCTCTACAG  
381 D I A V E W E S N G Q P E N N Y K T T P P V L D S D G S F F L Y S

mboII  
bpuAI

fnu4HI  
bsoFI  
bbvI

nlaIII  
ppu10I  
nsII/avaIII

sapi

mboII mnII

dsal

hphI

bspMI

asp700

nlaIII

sfaNI

sapi

mboII mnII

2601 CAAGCTCACC GTGGACAAGA GCAGGTGGCA CGAGGGGAGC GTCTCTCAT GCTCCGTGAT GCATGAGGCT CTGCACAACC ACTACACGCA GAAGAGCCTC  
414 K L T V D K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L

FIG. 48I



2701 TCCCTGCTC CCGGTAATG AGTGGGACGG CCTAGAGTC GACCTGCAGA AGCTTGGCGG CCATGGCCCA ACTTGTTTAT TGCAGCTTAT AATGGTTACA  
 AGGGACAGAG GCCATTAC TCACGCTGCC GGGATCTCAG CTGGACGTCT TCGAACCGGC GGTACGGGT TGAACAATA ACGTCGAATA TTACCAATGT

447 S L S P G K O

scrFI  
 nciI  
 mspI  
 hpaII  
 dsav  
 bsmAI  
 bali  
 caulI

taqI

pleI

rmalI  
 maeI  
 hincII/hindII

hinfI  
 pti  
 bsgI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
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 bsaJI

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 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
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hincII/pali  
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hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

hincII/pali  
 bsmI  
 hincII/bglI  
 bsaJI

FIG. 48J

2801 AATAACCAA TAGCATCACA AATTTCACAA ATAAAGCATT TTTTCACTG CATTCTAGTT GTGGTTGTC CAAACTCATC AATGTATCTT ATCATGTCTG  
 TTATTTCGTT ATCGTAGTGT TTAAGTGTT TATTTCGTAA AAAAGTGAC GTAAGATCAA CACCAACACAG GTTGAGTAG TTACATAGAA TAGTACAGAC

sau3AI  
 mboI/ndeII(dam-)  
 dpnI(dam+)  
 dpnII(dam-)  
 pvuI/bspCI  
 mcrI  
 bseI

taqI(dam-)  
 claiI/bsp106(dam-)  
 bspDI(dam-)  
 sau3AI  
 mboI/ndeII(dam-)  
 dpnI(dam+)  
 dpnII(dam-)  
 GATCGATCGG GAATTAATTC GCGGCAGCAC CATGGCCTGA AATAACCTCT GAAAGAGGAA CTGGGTTAGG TACCTTCTGA GCGGGAAGA ACCATCTGTG

fnu4HI  
 bsoFI  
 styI  
 bsvI  
 ncoI  
 hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
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 haeIII/pali

hincPI  
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 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

hincPI  
 dsal  
 haeIII/pali

rsal  
 csp6I  
 nlaIV  
 kpnI  
 hgiCI  
 banI

asp718  
 acc65I  
 ddeI  
 acII

asp718  
 acc65I  
 ddeI  
 acII

asp718  
 acc65I  
 ddeI  
 acII

asp718  
 acc65I  
 ddeI  
 acII

asp718  
 acc65I  
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asp718  
 acc65I  
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asp718  
 acc65I  
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 acII

asp718  
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asp718  
 acc65I  
 ddeI  
 acII

asp718  
 acc65I  
 ddeI  
 acII

asp718  
 acc65I  
 ddeI  
 acII





```

sau96I      nlaIII      styI
avaII
asuI
scrFI      nlaIII      styI
mvaI      clai/bsp106  pflMI
ecorII     sfaNI      ncoI
dsav      fnu4HI     ecoRI      dsaI      foki
bstNI      bsoFI      taqI      apoI      bsaJI      foki
apyI[dcM+] mnlI      bsh1236I aluI      bsaJI      bspDI[dam-] bsaJI
bsaJI      bsaJI      nruI      aluI      bsaJI      bspDI[dam-] bsaJI
3501 CCACCTTTTC TTTTCTCCA CAGGTGTCCA CTCCCAGGTC CAACTGCACC TCGGTTGCGG AAGCTAGCTT GGGCTGCATC GATTGAATTC CACCATGGGA
GGTGAAAAAG AAAACAGAGT GTCCACAGGT GAGGGTCCAG GTGACGTGG AGCCAGCGC TTGCATCGAA CCCGACCTAG CTAACCTAAG GTGGTACCCT
^cloning linker

```

```

alul
setI
sacI
hglJII
hgiAI/aspHI
ecII36II
bsp1286
bsiHRAI
bsmFI bmyI
alul
setI
sacI
hglJII
hgiAI/aspHI
ecII36II
bsp1286
bsiHRAI
bsmFI bmyI
bsrI avai
tthIII/aspI banII
acII
3601 TGGTCATGTA TCATCCCTTT TCTAGTAGCA ACTGCAACTG GAGTACATTC AGATATCCAG ATGACCCAGT CCGGAGCTC CCTGTCCGCC TCTGTGGCG
ACCACTACAT AGTAGGAAAA AGATCATCGT TGACGTTGAC CTCATGTAAG TCTATAGGTC TACTGGGTCA GGGCTCGAG GGACAGCGG AGACACCCGC
D I Q M T Q S P S L S A S V G D
1

```

```

scfI
pstI
bsgI
sse8387I
hphI
maeIII
bspMI
bsteII hphI bspMI
3701 ATAGGGTCAC CATCACCTGC AGGTCAAGTC AAGCTTAGT ACATGGTATA GGTGCTACGT ATTTACTACTG GTATCAACAG AAACCCAGGA AAGCTCCGA
TATCCCACTG GTAGTGGACG TCCAGTTGAG TTTCGAATCA TGTACCATAT CCAGGATGCA TAAATGTGAC CATAGTTGTC TTGGTCCCTT TTCGAGGCTT
18 R V T I T C R S S Q S L V H G I G A T Y L H W Y Q Q K P G K A P K

```

FIG. 48M



[illegible]

**FIG. 480**







5001 TGGCGTTACC CAACTTAATC GCCTTGCAGC ACATCCCCC TTCCGCCAGCT GCGGTAATAG CGACACCGCC CGACACCGATC GCGTGGCTAG CCGGAAGGGT. TGTCACACGCA

5001 TGGCGTTACC CAACTTAATC GCCTTGCAGC ACATCCCCC TTCCGCCAGCT GCGGTAATAG CGACACCGCC CGACACCGATC GCGTGGCTAG CCGGAAGGGT. TGTCACACGCA

5101 AGCCTGATG GCGAATGCG CCTGATGCGG TATTTCTCC TTACGCATCT GTGGGTAIT TCACACCGCA TAGCTCAAG CAACCATAGT ACGCGCCCTG  
TCGGACTTAC CGCTTACCG GGAATACGCC ATAAAGAGG AATGCGTAGA CACGCCATAA AGTGTGGCT ATGCAGTTTC GTTGGTATCA TCGCGGGGAC

5201 TAGCGCGGCA TTACGCGCG GCGGTGTGGT GGTACGCGC AGCGTACCG CTACACTGC CAGCGCCCTA GCGCGCGCTC CTTTGGCTTT CTTCCTTCC  
ATCGCGCGT AATTGCGGC GCCACACCA CCAATGCGG TCGCACTGC GATGTGACG GTGCGGGAT CCGCGCGGAG GAAAGCGA GAAGGAGG

FIG. 48R

mspI nlaIV hgiJII taqI  
 hpall hgiCI bniI mnlI  
 nael bsp1286  
 cfr10I/bsrFI bmyI  
 maeII cac8I aluI nlaIV  
 5301 TTTCTCGCCA CGTTGCGCGG CTTTCCCGCT CAAGCTCTAA ATCGGGGGCT CCCTTTAGG TTCCGATTTA GTGCTTTAGC GCACCTCGAC CCAGAAAAC  
 AAGAGCGGT GCAAGCGGC GAAAGGGCA GTTCGAGATT TAGCCCCCGA GGAATCC ARGCTAAT CAGGAATGC CGTGGAGCTG GGGTTTTTGTG  
 maeII haeIII/palI maeII pleI tru9I pleI  
 draII sau96I drdI hinfI maeII mseI hinfI  
 baeAI asuI  
 hphI  
 5401 TTGATTGGG TGATGGTTCA CGTAGTGGC CATGCCCTG ATAGACGTT TTTCGCCCTT TGACGTTGGA GTCCACGTTT TTTAATAGTG GACTCTTGT  
 AACTAAACC ACTACCAAGT GCATCACCCG GTAGCGGAC TATCTGCCA AAAGCGGAA ACTGCACCT CAGTGCAAG AATTATCAC CTGAGAACA  
 bsrI bslI bslI avai haeIII/palI aluI mseI tru9I mseI  
 5501 CCAAACTGA ACAACACTCA ACCCTATCTC GGGTATTCT TTTGATTAT AAGGATTTT GCCGATTTCG GCCTATTGGT TAAAAAATGA GCTGATTAA  
 GGTTCACCT TGTGTGAGT TGGGATAGAG CCGGATAAGA AACTAATA TTCCCTAAA CGGCTAAGC CGGATAACCA ATTTTACT CGACTAAT  
 thal fnuDII/mvni maeII bsp1286 acII fnu4HI bsoFI tru9I mseI  
 apoI apoI tru9I psp1406I  
 maeI bstUI mseI tru9I  
 bstUI bsh1236I aspi mseI  
 apoI bsh1236I  
 5601 CAAAAATTA ACGCAATTT TAACAAATA TTAACGTTTA CAATTTTATG GTGCACTCTC AGTACAATCT GCTCTGATGC CGCATAGTTA AGCCAACTCC  
 GTTTTAAAT TCGCTTAA ATGTTTAT AATTGCAAT GTTAAATAC CACGTGAGAG TCATGTTAGA CGAGACTAGC GGTATCAAT TCGTTGAGG  
 hinPI hhaI/cfoI  
 thal fnuDII/mvni  
 fnu4HI bstUI  
 maeIII maeII bsrI nlaIII hhaI/cfoI nspBII bsh1236I  
 baeAI tthlII/aspi bbvI acII hgal drdI  
 5701 GGTATCGCTA CGTACTGGG TCATGGCTC GCCCGACAC CCGCTGACCG GCGCTGACCG GCTTGTCTGC TCCGGCATC CGCTTACAGA  
 CGATAGCGAT GCACTGACCC ACTACCGAG CGGGGTGTG GCGACTGCG CGGACTGCC CGAAGACAG AGGCCGTAG CGAATGTCT

FIG. 48S

5801 CAAGCTGTGA CCGTCTCCGG GAGCTGCATG TGTACAGAGGT TTTCACCGTC ATCACCAGAA CGCGGAGGC AGTATTCTTG AAGACGGAAG GGCCTCGTGA  
 GTTCGACACT GGCAGAGGCC CTCGACGTAC ACAGTCTCCA AAGTGGCAG TAGTGGCTTT GCGCGCTCCG TCATAAGAAC TTCTGCTTTC CCGGAGCACT  
 5901 TACGCCCTATT TTTATAGGTT AATGTCATGA TAATAATGGT TTCTTAGACG TCAGGTGGCA CTTTTCGGGG AAATGTGCGC GGAACCCCTA TTTGTTTATT  
 ATCGGGATAA AATATCCAA ATACAGTACT ATTATTACCA AAGAATCTGC AGTCCACCGT GAAAAGCCCC TTTACACGCG CTTGGGGAT AAACAATAA  
 6001 TTTCTAAATA CATTCAAATA TGTATCCGCT CATGAGACAA TAACCTCGAT AAATGCTTCA ATATATTGA AAAAGGAAGA ATATGAGTAT TCAACATTTC  
 AAAGATTAT GTAAGTTAT ACATAGGCCA GTACTCTGTT ATTGGGACTA TTTACGAAGT TATTATNACT TTTTCTTCT CATACTATA AGTTGTAAG  
 6101 CGTGTGCCCC TTATTCCTT TTTTGGCGGA TTTTGCTTC CTGTTTTGC TCACCCAGAA ACCTGGTGA AGATAAAGA TGCTGAAGT CAGTTGGGTG  
 GCACAGCGGG AATAGGGAA AAAACGCCGT AAAACGGAAG GACAAAACG AGTGGGTCTT TGGACCACT TTCAATTTCT ACAGTTCTA GTCACCCAC

FIG. 48T

6001 CACGAGTGGG TTACATCGAA CTGGATCTCA ACAGCGGTAA GATCCTTGAG AGTTTTCGCC CCGAAGAACG TTTTCCAATG ATGAGCACTT TTAAAGTTCT

6201 CACGAGTGGG TTACATCGAA CTGGATCTCA ACAGCGGTAA GATCCTTGAG AGTTTTCGCC CCGAAGAACG TTTTCCAATG ATGAGCACTT TTAAAGTTCT  
 GTGCTCACCC AATGTAGCTT GACCTAGAGT TGTGGGCATT CTAGGAACCTC TCAGAACGCGG GGCCTTCTGC AAAAGGTTAC TACTCGTGAA AATTTCACAA

scfPI  
 aciI  
 thal  
 fnuDII/mvni  
 bstUI  
 bsh1236I  
 hinPI  
 hhal/cfoI

6301 GCTATGTGGC GCGGTATTAT CCGGTGATGA CGCCGGGCAA GAGCAACTCG GTCCGGCGCAT ACACATATTCT CAGAACTGACT TGCTTGAGTA CTCACCACTC  
 CGATACACCG CGCCATAATA GGGCACTACT GCGGCCCGTT CTGCTTGACC CAGCGGCGTA TGTGATNAGA GTCTTACTGA ACCAACTCAT GAGTGGTCTAG

6401 ACAGAAAGC ATCTTACGGA TGGCATGACA GTAAGAGAAAT TATGAGTGC TGCCATAACC ATGAGTGATA ACACCTGCGC CAACCTACTT CTGACACAGA  
 TGTCTTTTCG TAGAATGCCT ACCGTACTGT CATTCTCTTA ATAGTCACG ACGGTATTGG TACTCACTAT TGTGACGCGG GTTGAATGAA GACTGTTGCT

6501 TCGGAGGACC GAAGGAGCTA ACCGCTTTT TGCACAACAT GGGGATCAT GTAACCTGCC TTGATCGTTG GGAACCGGAG CTGAATGAAG CCATACCCAA  
 AGCTCCTCGT CTTCCTCGAT TGGGGAATAA ACGTGTGTA CCCCCTAGTA CATTGACGCG AACTAGCAAC CTTGGGCTC GACTTACTTC GGTATGGTTT

FIG. 48U

6601 CGACGACGGT GACACCACGA TGCCAGCAGC AATGGCAACA ACCTTGCGCA AACTATTAC TGGCGAATA CTACTCTAG CTTCCCGCA ACAATTATA  
 GCTGCTCGCA CTGTGGTCT ACGTCTGCT TACCGTGT TGAACGCGT TGTATAATTG ACCGCTTAT GAATGAGATC GAAGGCGGT TGTAAATTAT

6701 GACTGGATGG AGGGGATAA AGTTGCAGCA CCACCTCTGC GCTCGGCGCT TCCGGCTGGC TGGTTTATTG CTGATAAATC TGGAGCCGT GAGCGTGGGT  
 CTGACCTACC TCCGCTATT TCAACGTCT TCAACGACG CGAGCCGCGA AGCCGACCG ACCAATAAC GACTATTAG ACCTCGGCA CTGCAACCCA

6801 CTCGCGGTAT CATTCAGCA CTGGGGCAG ATGGTAAGC CTCCGTCATC GTAGTTATCT ACACGACGG GAGTCAGGCA ACTATGGATG AACGAATAG  
 GAGCGCCATA GTAACGCTCT GACCCCGTC TACCATTGG GAGGCGATAG CATCAATAGA TGTGCTGCC CTCAGTCCCT TGAATCTTGA AGTAAATTT

6901 ACAGATCGCT GAGATAGGTG CCTCACTGAT TAAGCATGG TAACGTGTCAG ACCAAGTTA CTCATATATA CTTAGATTG ATTAAACT TCATTTTAA  
 TGTCTAGCGA CTCATCCAC CGAGTGACTA ATTCTGAACC ATTGACACTC TGGTTCAAT GAGTATAT GAAATCTAAC TAAATTTTGA AGTAAATTT

7001 TTTAAAGGA TTAGTGA GATCCTTTT GATAATCTA TGACCAAAAT CCTTAACGT GAGTTTCTG TCCACTGAGC GTCAGACCCC GTAGAAAGA  
 AAATTTTCT AGATCCACT CTAGGAANA CTATTAGAT ACTGGTTTA GGAATTGA CTTCAAGCA AGGTGACTC GAGTCTGGG CATCTTTCT

FIG. 48V

```

sau3AI
mboI/dam-]
sau3AI mboI/ndeII(dam-) thal
mboI/ndeII(dam-) fnuDII/mvni
dpmI(dam+) dpmI(dam+) bstUI cac8I
dpmII(dam-) dpmII(dam-) bsh1236I fnu4HI
bstYI/xhoII alwI(dam-) hinPI bsoFI
bstYI/dam-] bstYI/xhoII hhaI/cfoI bbvI
alwI(dam-) bstYI/xhoII hhaI/cfoI bbvI
7101 TCAAAGGATC TTCTTGAGAT CCTTTTTC TCGCGGTAAT CTGCTGCTTG CAAACAAAAC AACACCGCT ACCAGCGGTG GTTTGTTTGC CGGATCAAGA
AGTTTCCTAG AAGAACTCTA GGAAGAAAAG ACGCGCATTA GACGACGAAC GTTTGTTTTT TTGCTGGCGA TGGTCGCCAC CAAACAAAACG GCTAGTTCT
7201 GCTACCAACT CTTTTCCGA AGGTAACTGG maeIII bsrI hinPI hhaI/cfoI rmaI haeIII/palI
CGATGCTGA GAAAAGGCT TCCATTGACC GAAGTCGTCT CCGCTCTATG bfaI bsaI haeI
7301 TCTGTAGCAC CGCCTACATA CCTCGCTCTG CTAATCCTGT TACCAGTGGC TGCTGCCAGT GCGGATAAGT CGTGCTTTAC CGGTTGGAC TCAACAGCAT
AGACATCGTG CGGATGTAT GGAGCGAGAC GATTAGGACA ATGGTCACCG ACGACGGTCA CCGCTATTCA GCACAGAATG GCCCAACCTG AGTTCTGCTA
7401 AGTTACCGGA TAAGCGCGAG CGGTGCGGCT GAACGGGGGG TTCTGCGACA CAGCCAGCT TGGAGCGAAC GACCTACACC GAAGTGAAT ACCTACAGCG
TCAATGGCCT ATTCCGGCTC GCCAGCCCGA CTGCCCCCCC AAGCAGCTGT CTCGGGTGCA ACCTCGCTTG CTGACTCTA TGGATGTCG

```

FIG. 48W



[illegible]

**FIG. 48Y**





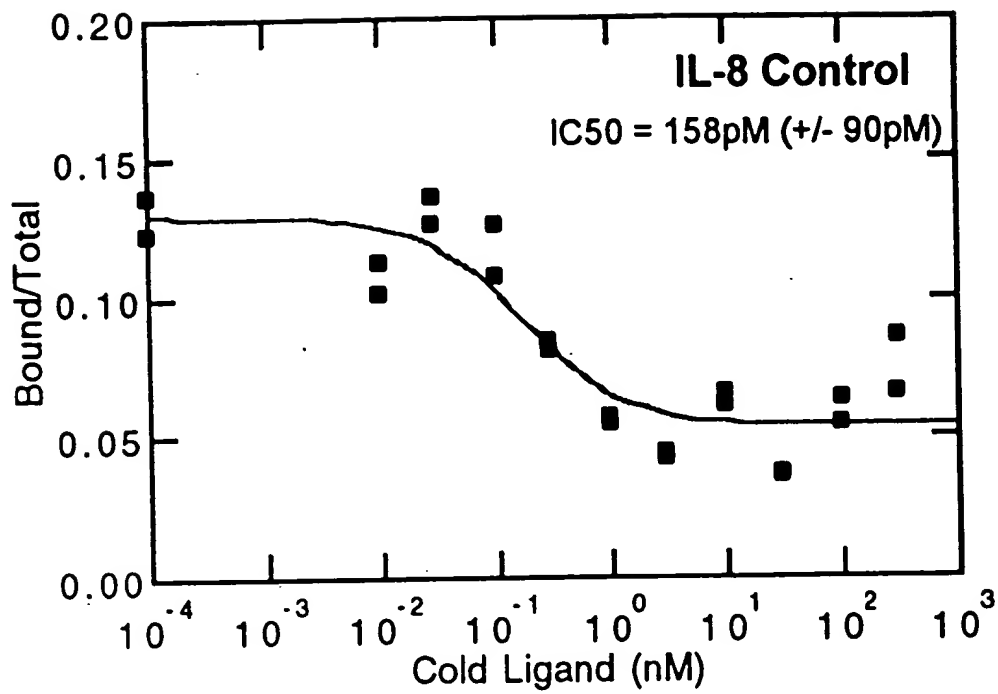


FIG. 49A

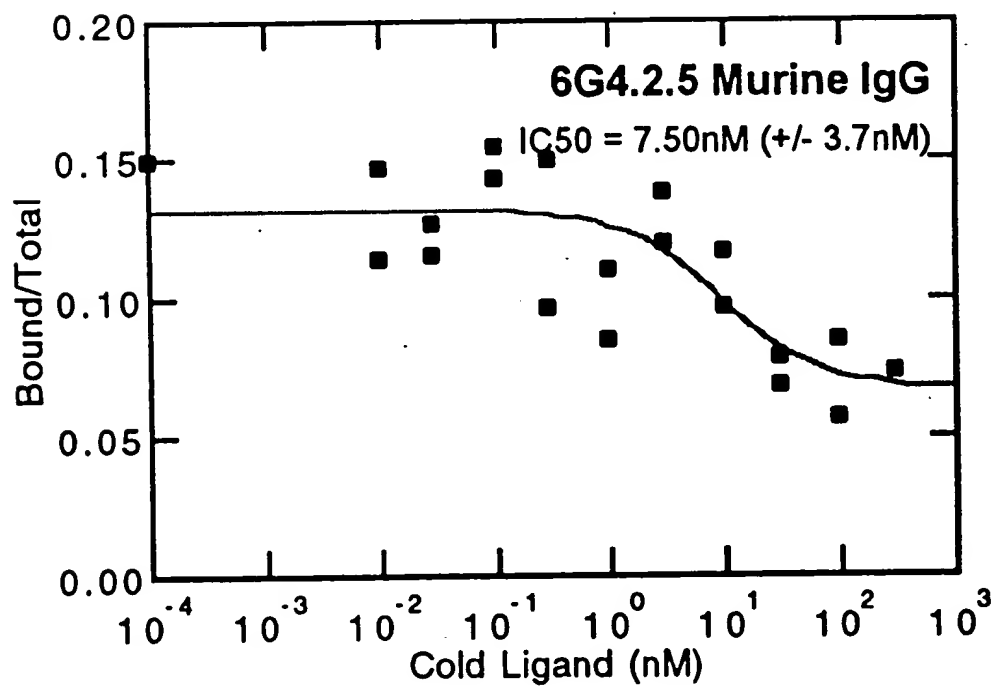


FIG. 49B

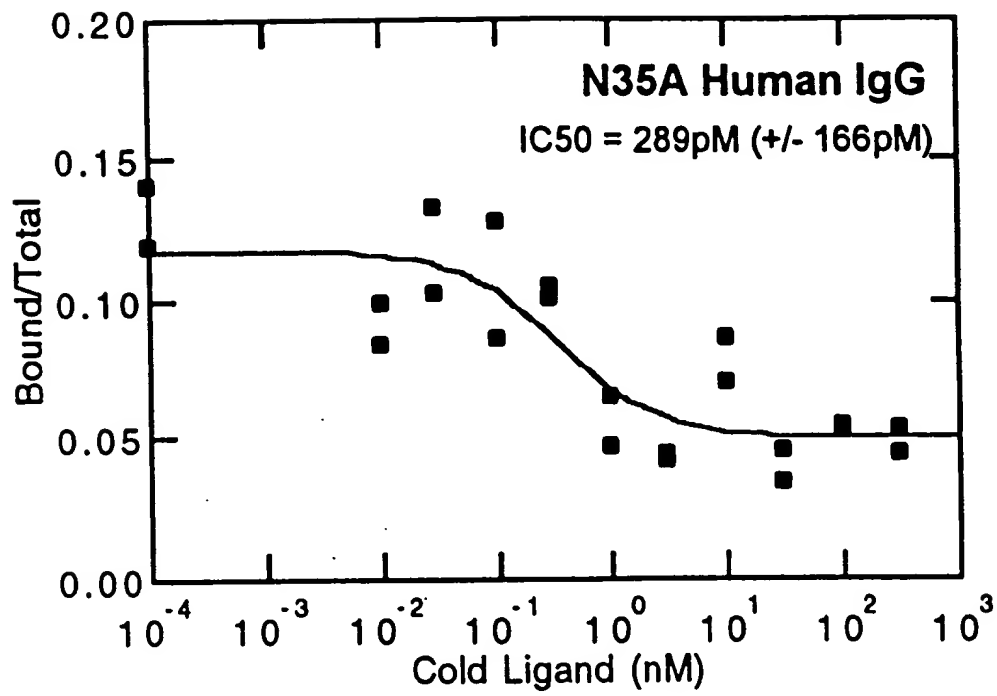


FIG. 49C

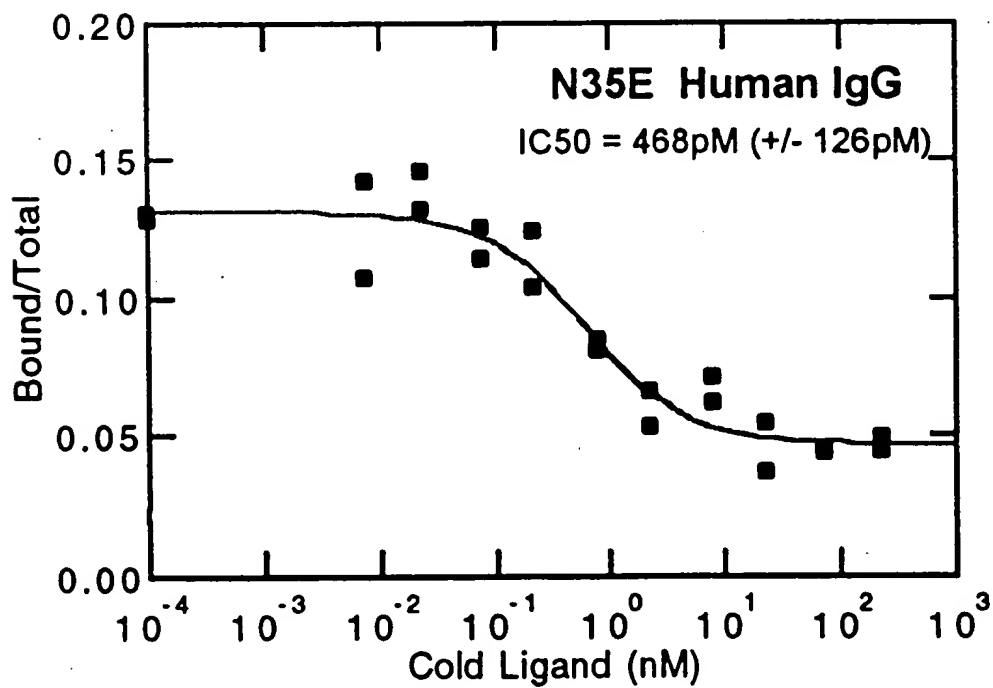


FIG. 49D

0.4nM N35E IgG

Pub  
B7

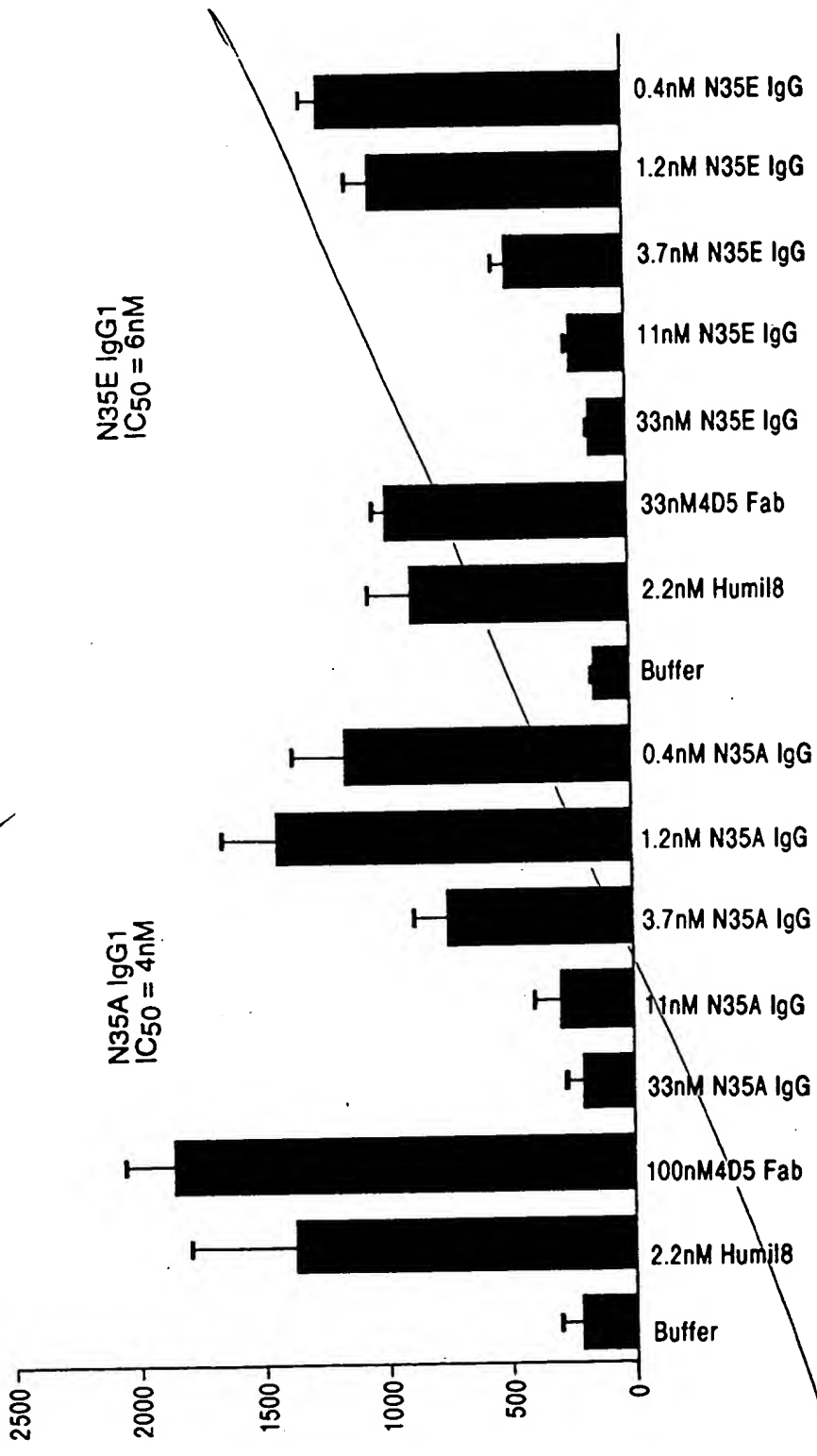


FIG. 50A

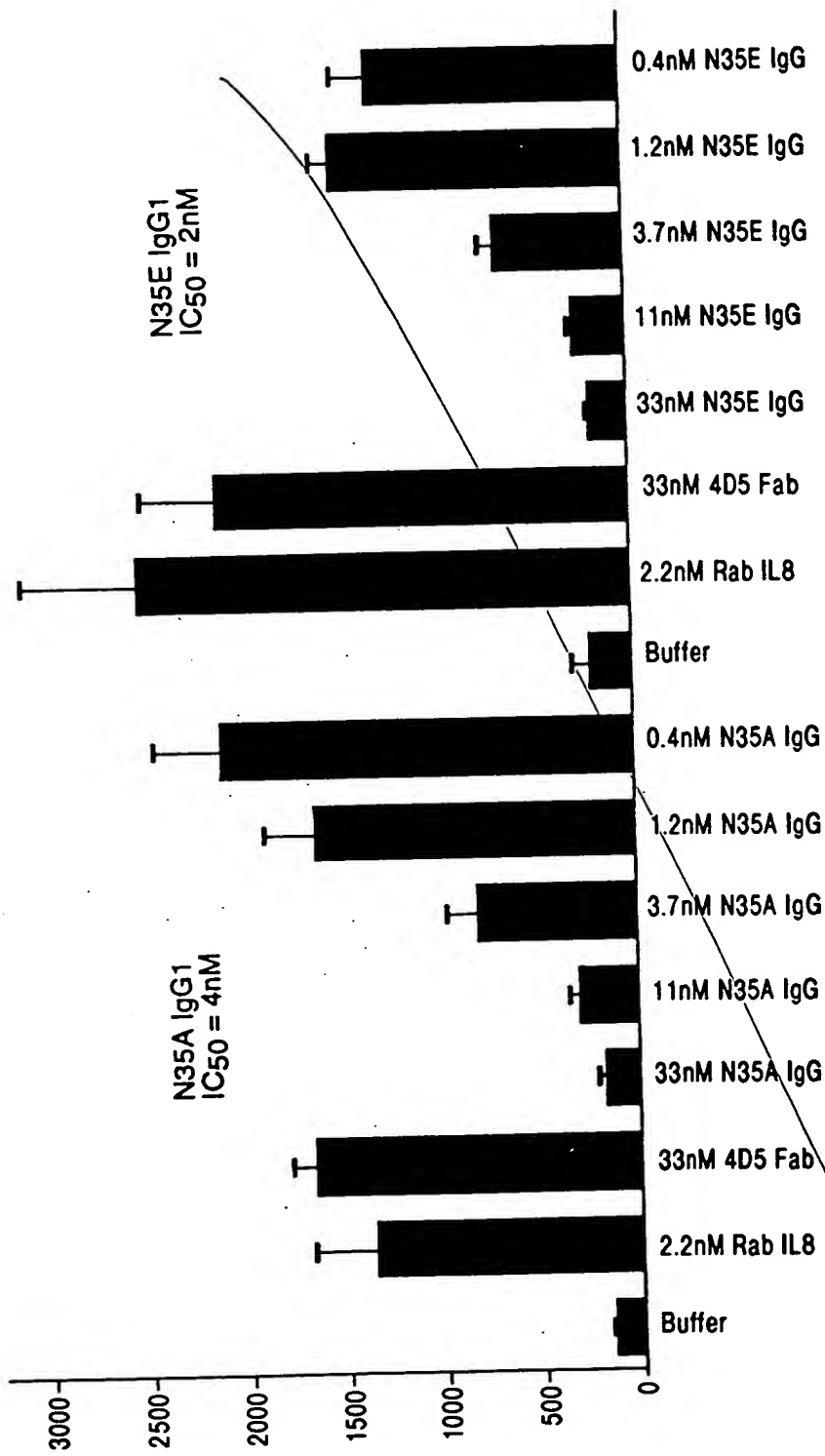
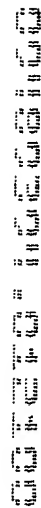


FIG. 50B



**FIG. 51**

**FIG. 51**

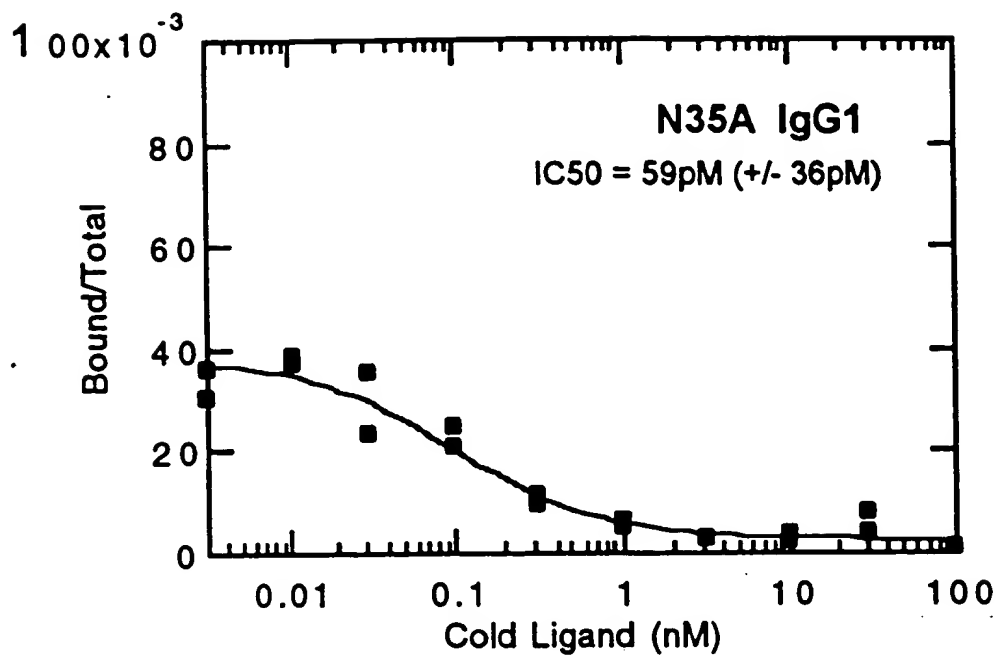


FIG. 52A

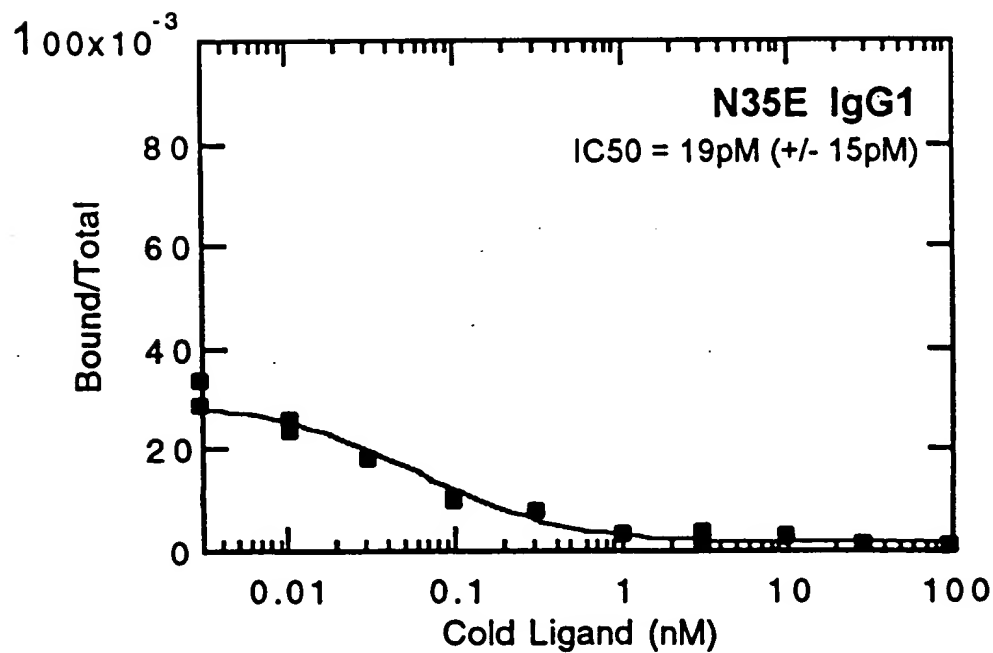


FIG. 52B

781 AAAAGGGTAT CTAGAGGTTG AGGTGATTTT ATGAAAAAGA ATATCGCATT TCTTCTTGCA  
 TTTTCCCATG GATCTCCAAC TCCACTAAAA TACTTTTTCT TATAGCGTAA AGAAGAACGT  
 -1 M K K N I A F L L A  
 841 TCTATGTTCTG TTTTTTCTAT TGCTACAAAC GCGTACGCTG AGGTTTCAGCT AGTGCAGTCT  
 AGATACAAGC AAAAAAGATA ACGATGTTTG CGCATGCGAC TCCAAGTCGA TCACGTCAGA  
 -11 S M F V F S I A T N A Y A E V Q L V Q S  
 901 GGCGGTGGCC TGGTGCAGCC AGGGGGCTCA CTCGTTTGT CCTGTGCAGC TTCTGGCTAC  
 CCGCCACCGG ACCACGTCGG TCCCCCGAGT GAGGCAAACA GGACACGTCG AAGACCGATG  
 8 G G G L V Q P G G S L R L S C A A S G Y  
 961 TCCTTCTCGA GTCATATAT GCACTGGGTC CGTCAGGCC CCGGTAAGGG CCTGGAATGG  
 AGGAAGAGCT CAGTGATATA CGTGACCCAG GCAGTCCGGG GCCCATTCCTC GGACCTTACC  
 28 S F S S H Y M H W V R Q A P G K G L E W  
 1021 GTTGGATATA TTGATCCTTC CAATGGTGAA ACTACGTATA ATCAAAAGTT CAAGGGCCGT  
 CAACCTATAT AACTAGGAAG GTTACCACTT TGATGCATAT TAGTTTTCAA GTTCCCGGCA  
 48 V G Y I D P S N G E T T Y N O K F K G R  
 1081 TTCACCTTAT CTCGCGACAA CTCCAAAAAC ACAGCATACC TGCAGATGAA CAGCCTGCGT  
 AAGTGAAATA GAGCGCTGTT GAGGTTTTTG TGTCGTATGG ACGTCTACTT GTCGGACGCA  
 68 F T L S R D N S K N T A Y L Q M N S L R  
 1141 GCTGAGGACA CTGCCGTCTA TTA CTGTGCA AGAGGGGATT ATCGCTACAA TGGTGA CTG  
 CGACTCCTGT GACGGCAGAT AATGACACGT TCTCCCTAA TAGCGATGTT ACCACTGACC  
 88 A E D T A V Y Y C A R G D Y R Y N G D W  
 1201 TTCTTCGACG TCTGGGGTCA AGGAACCCTG GTCACCGTCT CCTCGGCCTC CACCAAGGGC  
 AAGAAGCTGC AGACCCAGT TCCTTGGGAC CAGTGGCAGA GGAGCCGGAG GTGGTTCCCG  
 108 F F D V W G Q G T L V T V S S A S T K G  
 1261 CCATCGGTCT TCCCCCTGGC ACCCTCCTCC AAGAGCACCT CTGGGGGCAC AGCGGCCCTG  
 GGTAGCCAGA AGGGGGACCG TGGGAGGAGG TTCTCGTGGA GACCCCGTG TCGCCGGGAC  
 128 P S V F P L A P S S K S T S G G T A A L  
 1321 GGCTGCCTGG TCAAGGACTA CTTCCCCGAA CCGGTGACGG TGTCGTGGAA CTCAGGCGCC  
 CCGACGGACC AGTTCTGAT GAAGGGGCTT GGCCACTGCC ACAGCACCTT GAGTCCGCGG  
 148 G C L V K D Y F P E P V T V S W N S G A  
 1381 CTGACCAGCG GCGTGACAC CTTCCCGGCT GTCCTACAGT CCTCAGGACT CTACTCCCTC  
 GACTGGTTCG CGCACGTGTG GAAGGGCCGA CAGGATGTCA GGAGTCTGA GATGAGGGAG  
 168 L T S G V H T F P A V L Q S S G L Y S L  
 1441 AGCAGCGTGG TGACCGTGCC CTCCAGCAGC TTGGGCACCC AGACCTACAT CTGCAACGTG  
 TCGTCGCACC ACTGGCACGG GAGGTCGTCG AACCCGTGGG TCTGGATGTA GACGTTGCAC  
 188 S S V V T V P S S S L G T Q T Y I C N V  
 1501 AATACAAGC CCAGCAACAC CAAGGTCGAC AAGAAAGTTG AGCCCAAATC TTGTGACAAA  
 TTAGTGTTCG GGTCGTTGTG GTTCCAGCTG TTCTTTCAAC TCGGGTTTAG AACACTGTTT  
 208 N H K P S N T K V D K K V E P K S C D K  
 1561 ACTCACACAT GCCCGCCGTGA  
 TGAGTGTGTA CGGGCGGCACT  
 228 T H T C P P O

FIG. 53



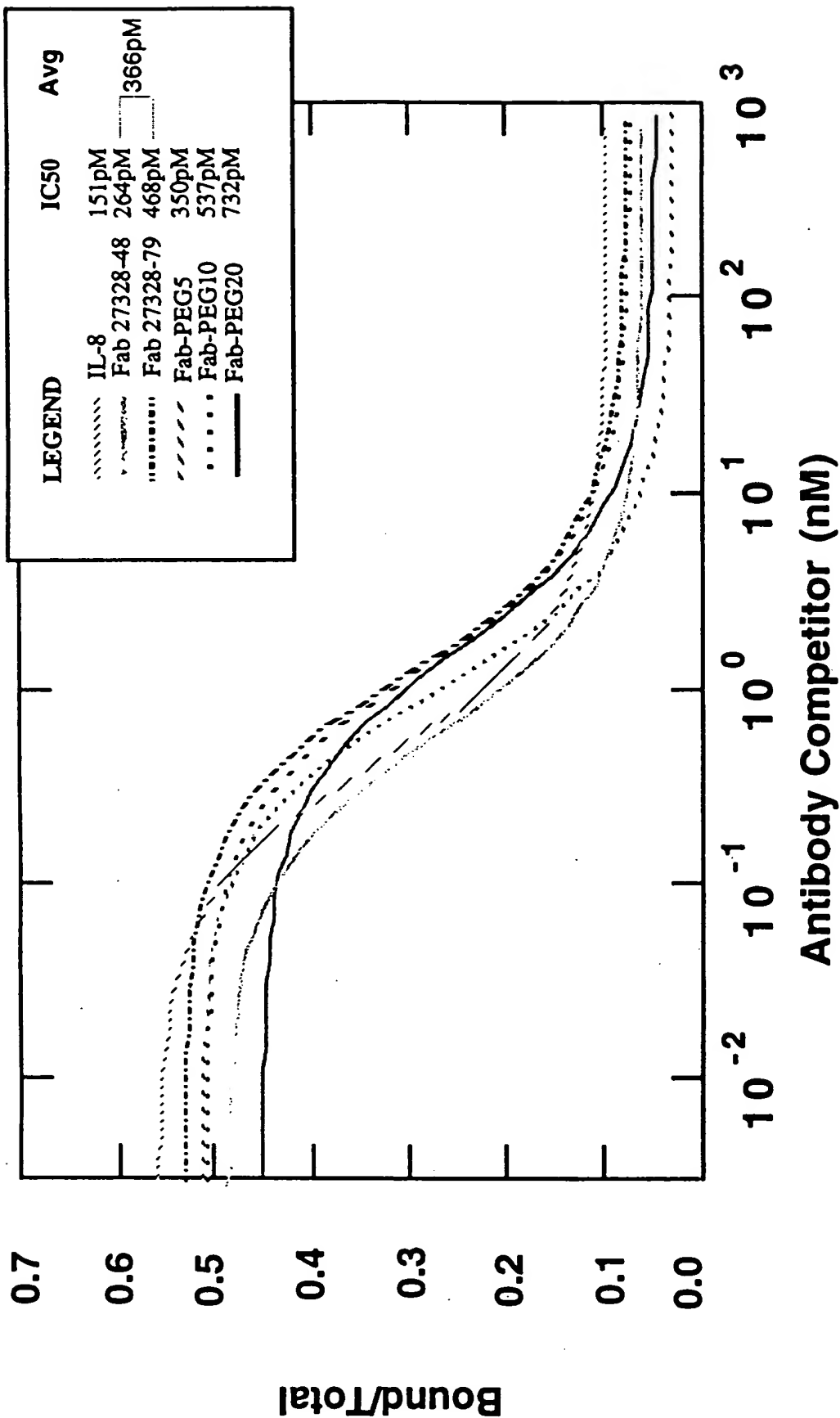


FIG. 54A

**LEGEND**

Line Style	IC50
Solid line	IL-8 363pM
Dashed line	Fab 27328-79 802pM
Dotted line	Fab-PEG30 624pM
Dash-dot line	Fab-PEG40 1.10nM

Antibody Competitor (nM)

**FIG. 54B**



0.4nM PEG20K Fab

B9

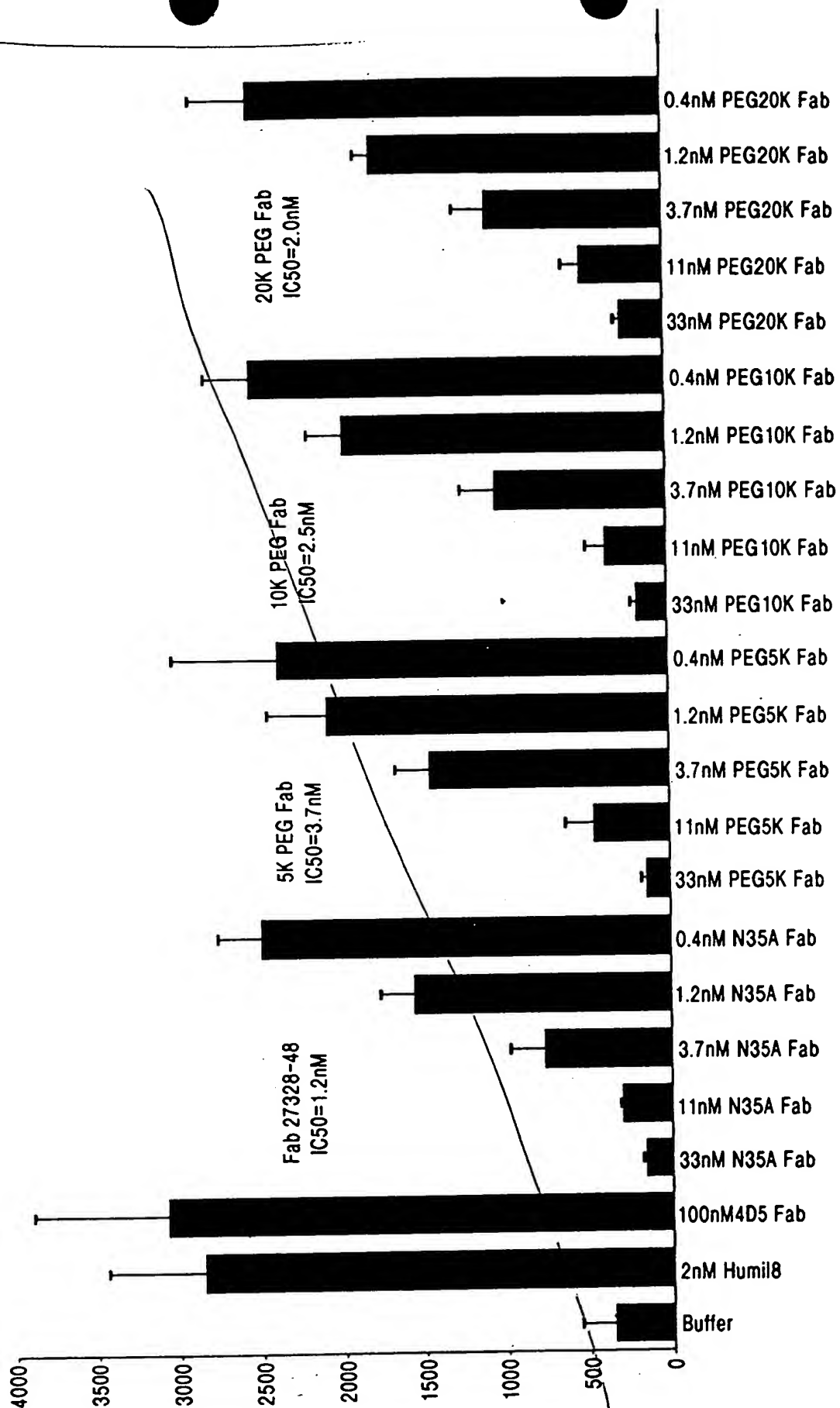


FIG. 55A

hnb  
B10

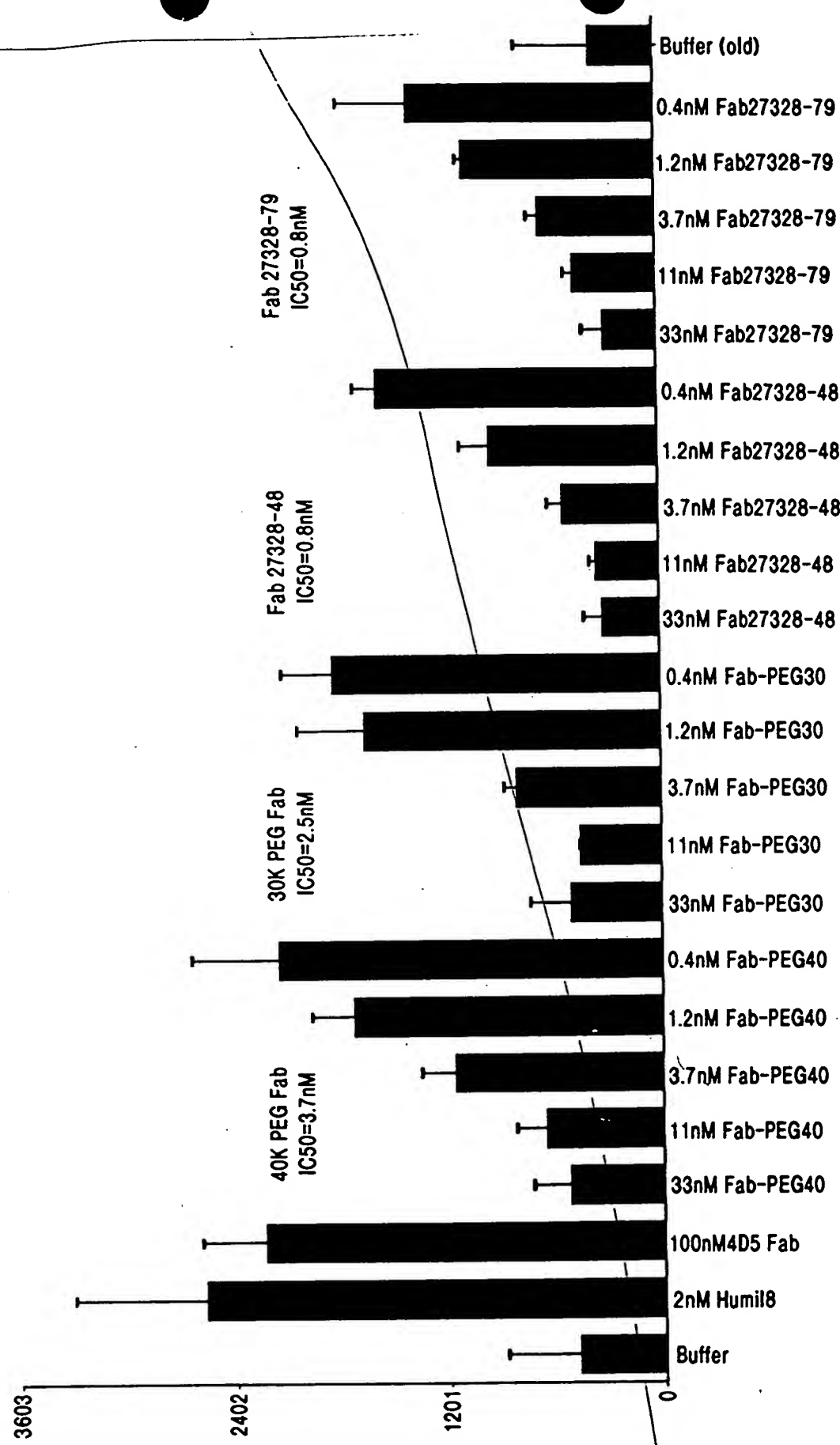


FIG. 55B

Cell to cell communication

Ant  
B11

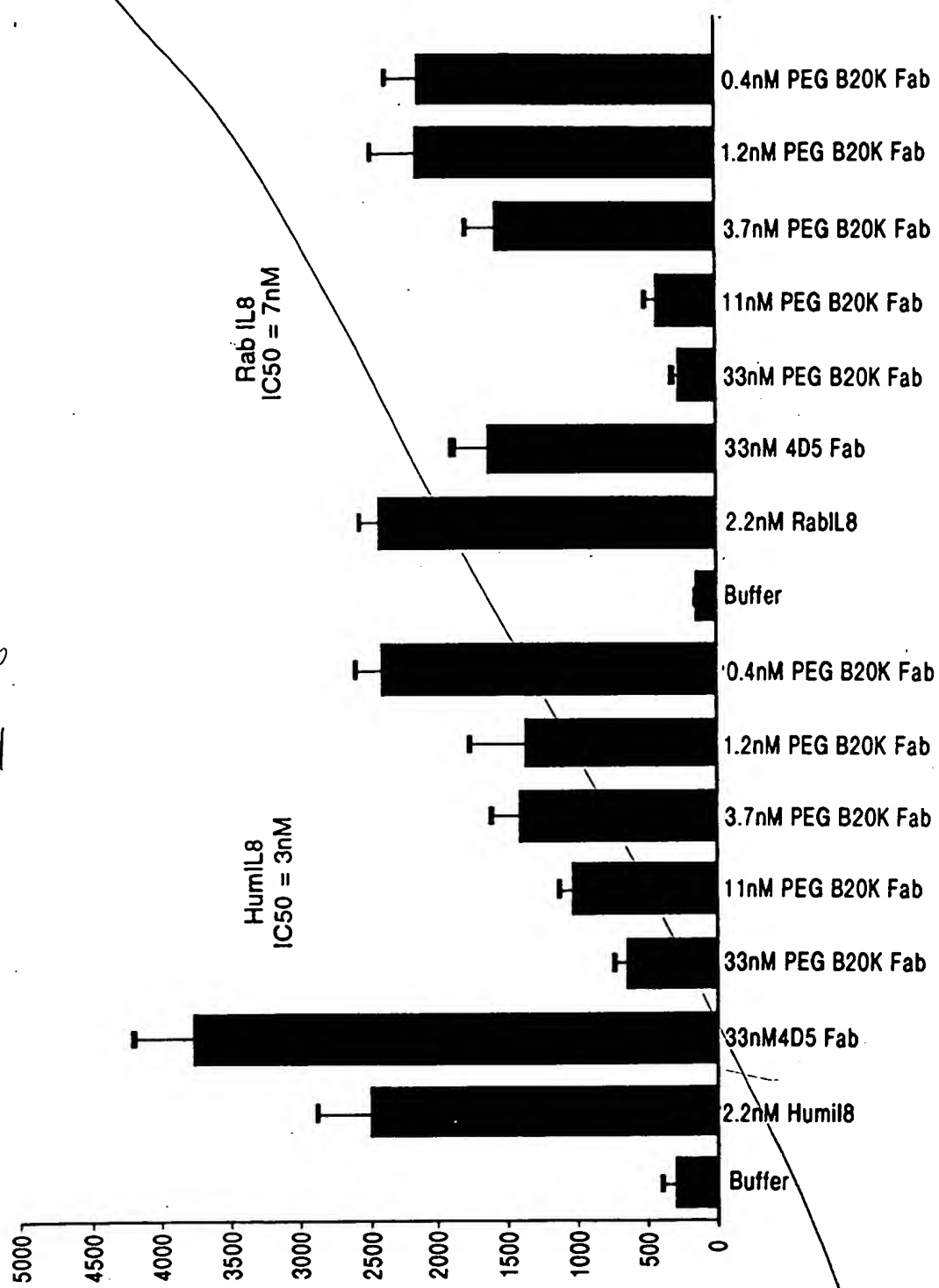
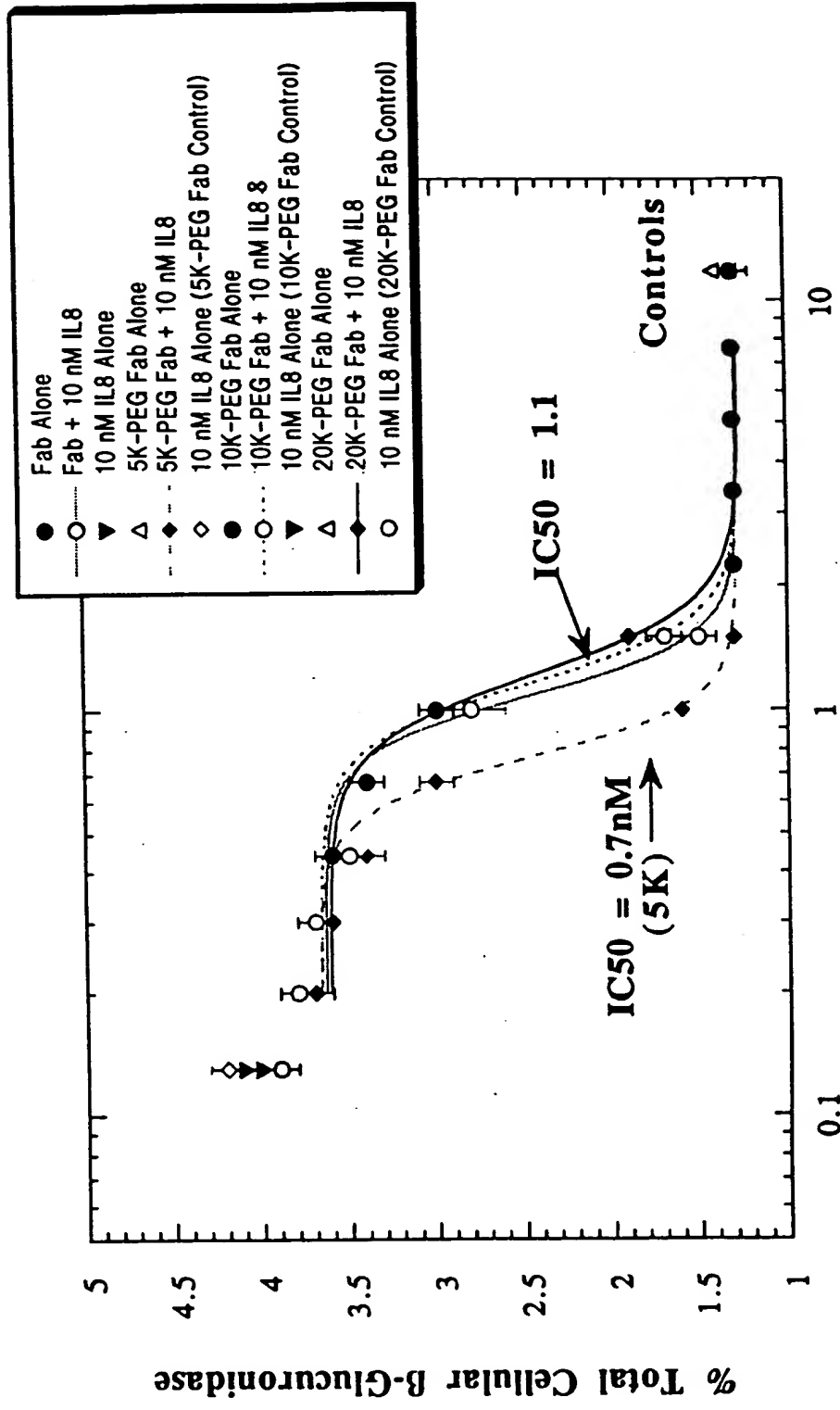


FIG. 55C



**Molar Ratio Antibody:IL-8**  
**FIG. 56A**

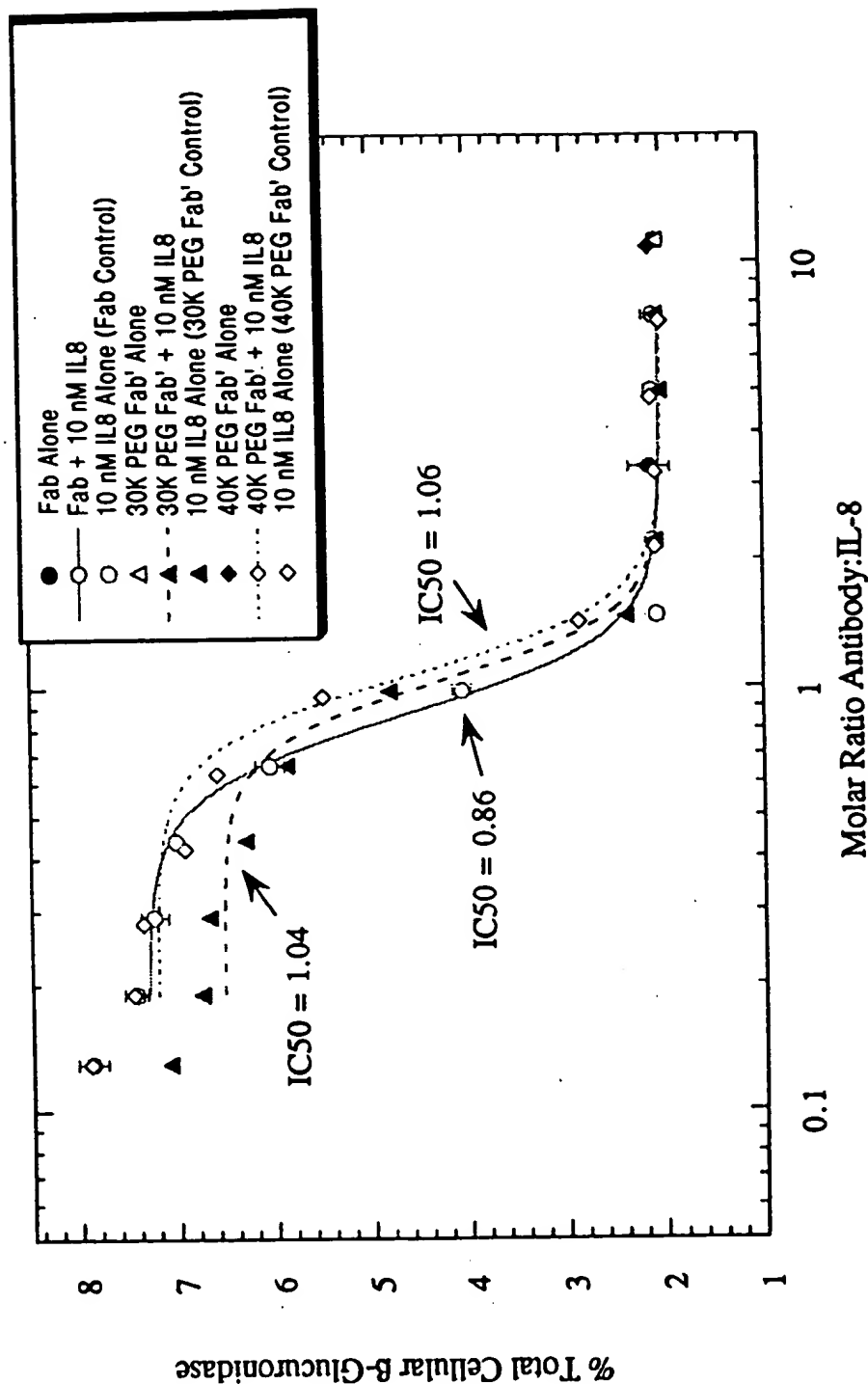
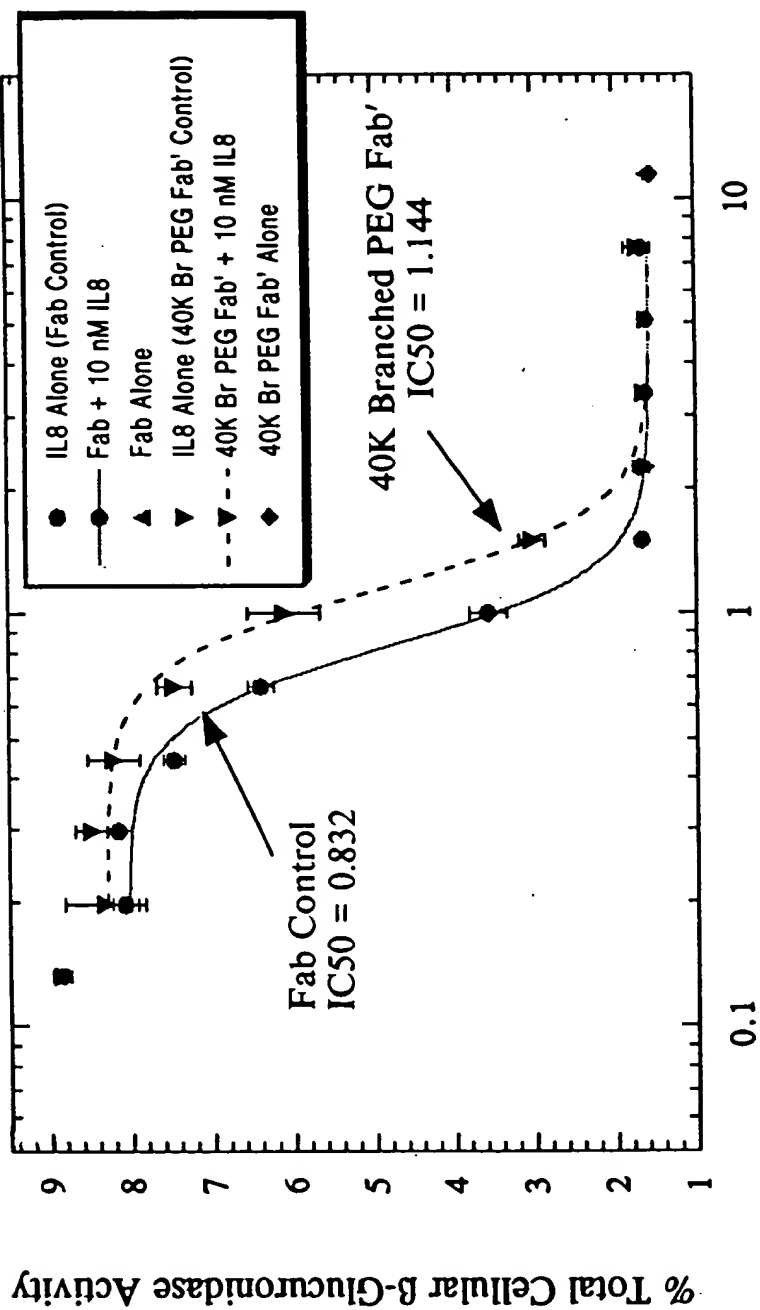


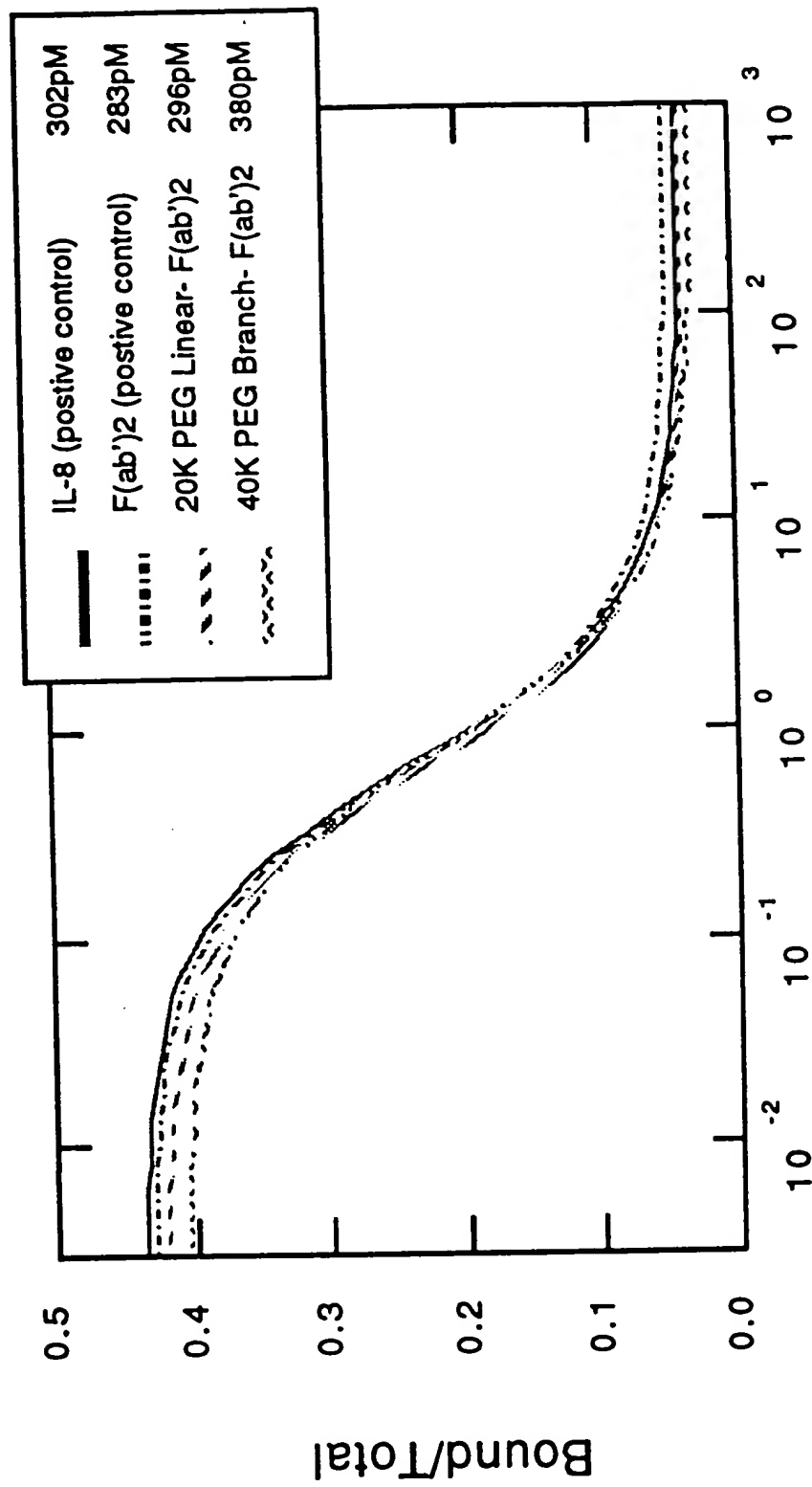
FIG. 56B





**FIG. 56C**

0.5 0.4 0.3 0.2 0.1 0.0



Pegylated F(ab')<sub>2</sub> (nM)

FIG. 57A

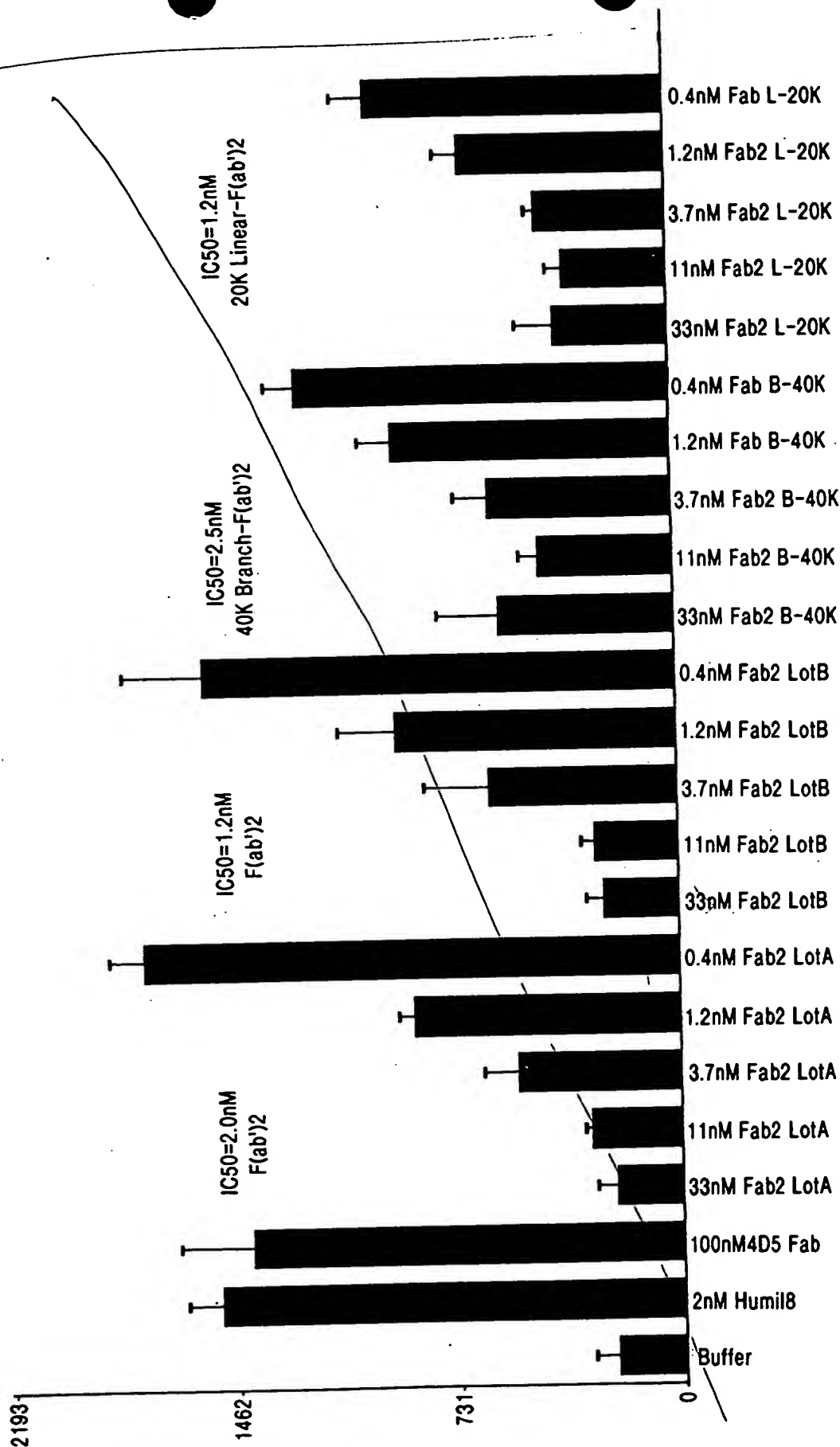
Figure 1 is a binding curve showing the ratio of bound to total antibody (Bound/Total) on the y-axis (ranging from 0.0 to 0.5) versus the log<sub>10</sub> concentration of the antigen on the x-axis (ranging from -3 to 3). The curves represent the binding of IL-8 to various F(ab')<sub>2</sub> antibodies. The legend indicates the following conditions:

- IL-8 (positive control): Solid line
- F(ab')<sub>2</sub> (positive control): Dotted line
- 20K PEG Linear (3,4,5)-F(ab')<sub>2</sub>: Dashed line
- 40K PEG (2) Branch-F(ab')<sub>2</sub>: Wavy line

The 20K PEG Linear (3,4,5)-F(ab')<sub>2</sub> and 40K PEG (2) Branch-F(ab')<sub>2</sub> curves show lower binding affinity compared to the positive controls, with the 40K PEG (2) Branch-F(ab')<sub>2</sub> curve showing the lowest binding.

**FIG. 57B**

Paul  
Blz



mb  
B13

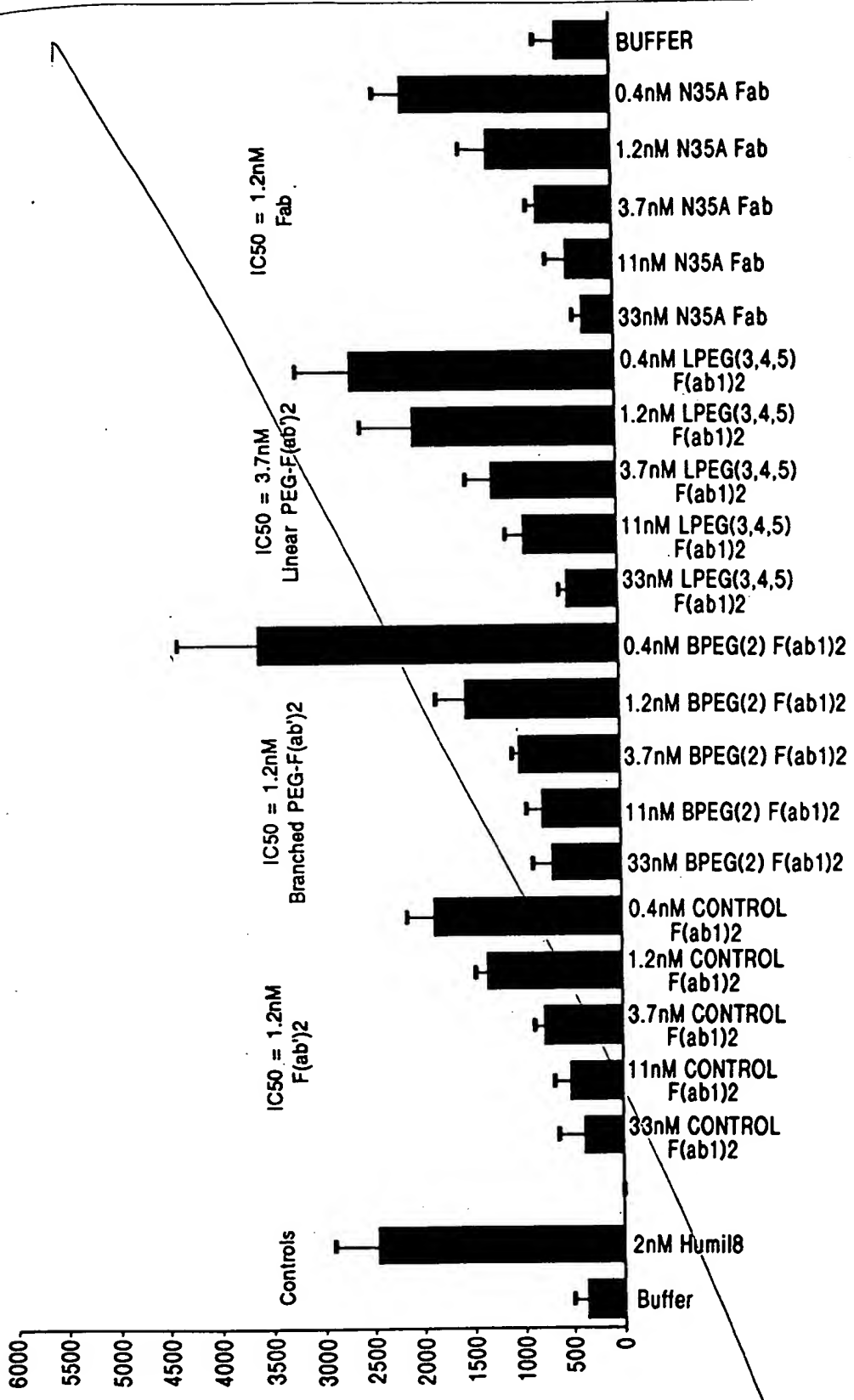


FIG. 58B

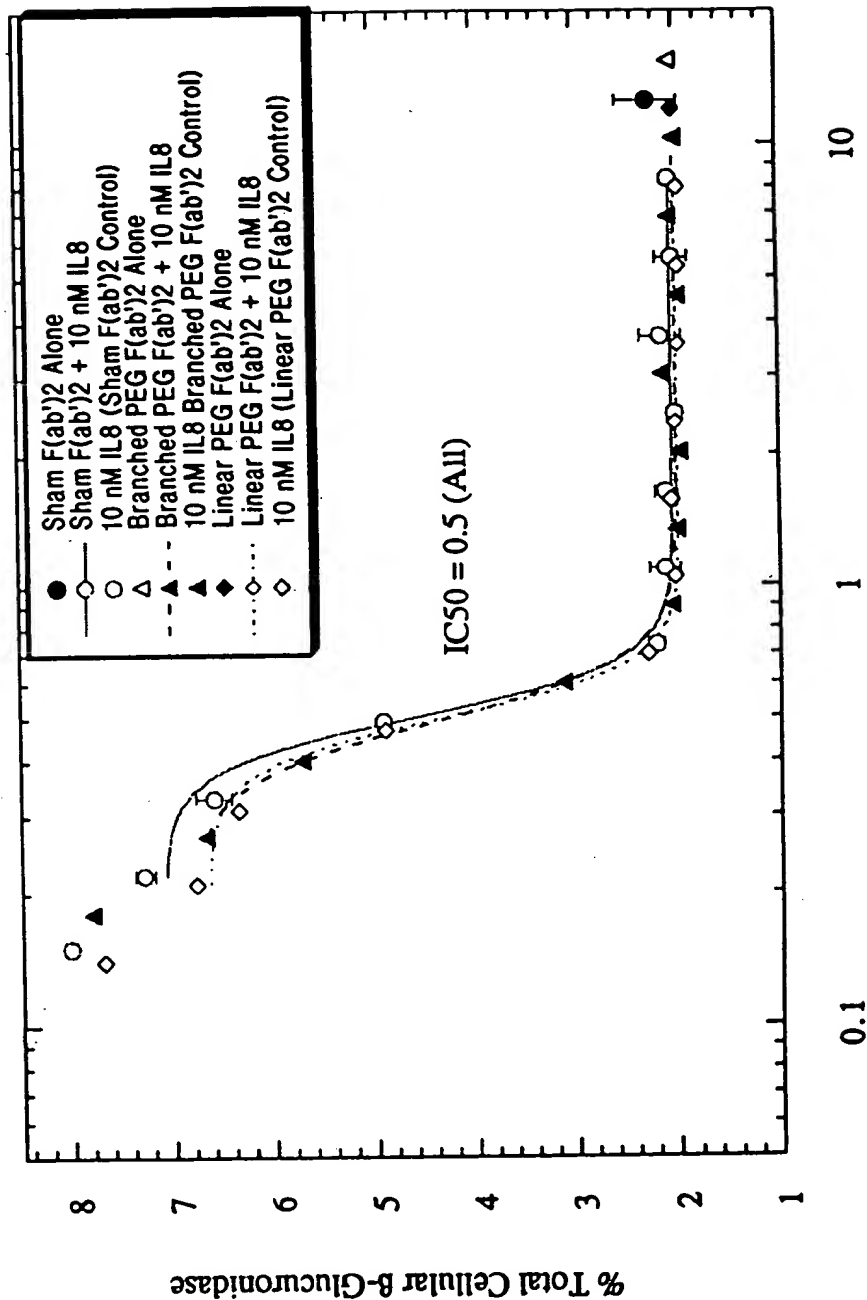
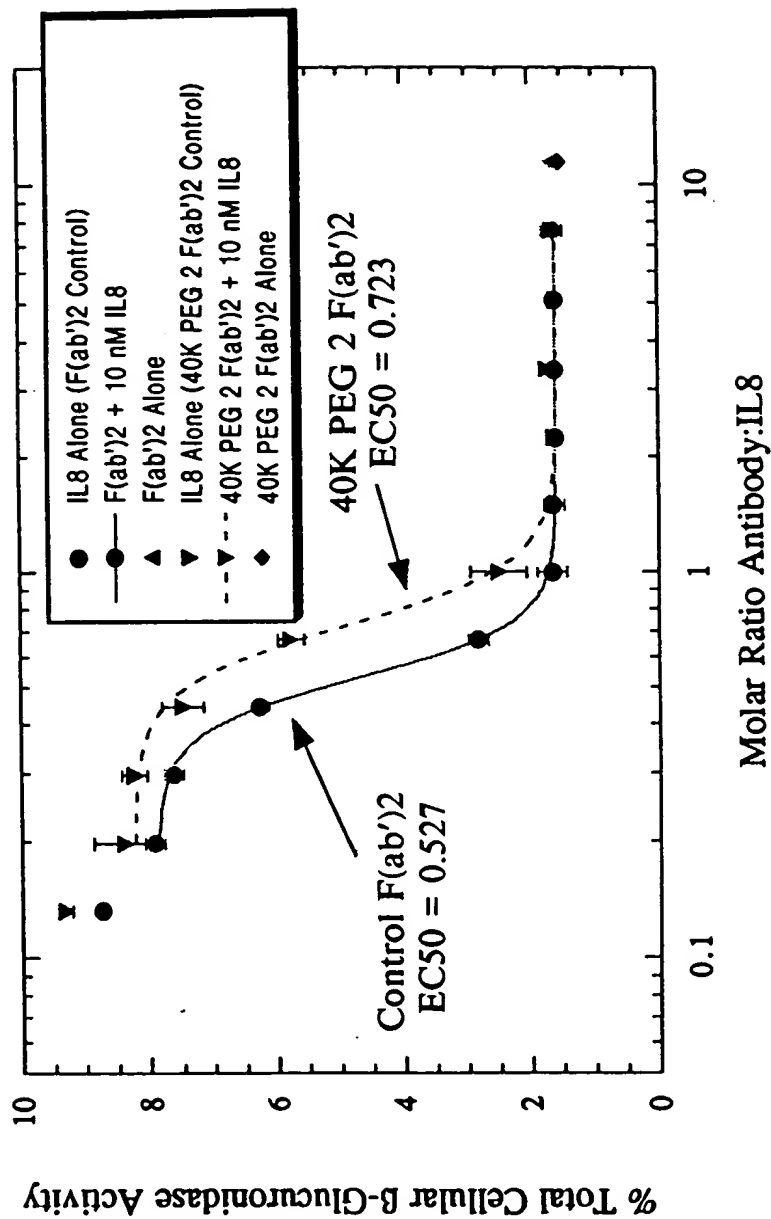


FIG. 59A



**FIG. 59B**

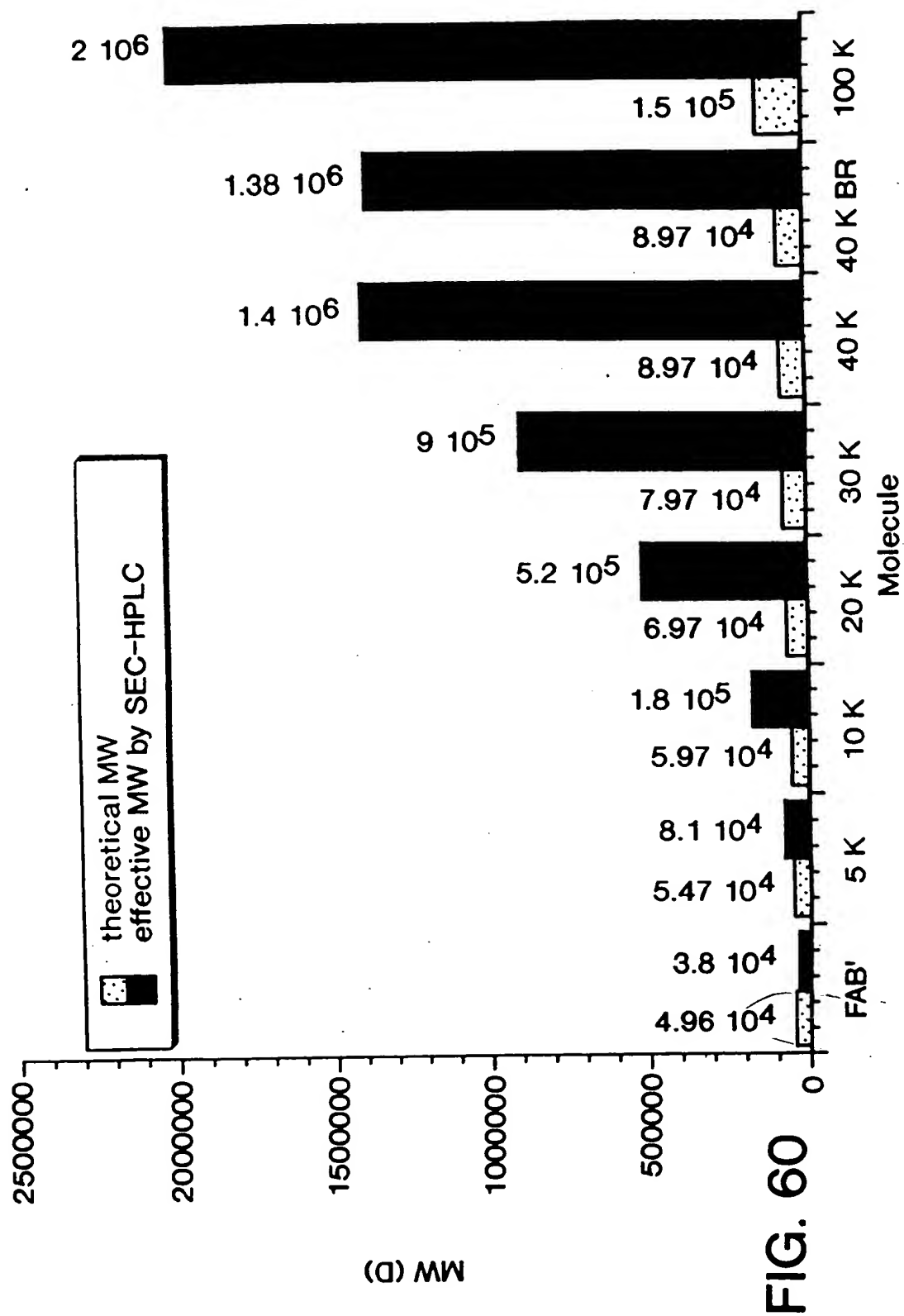




FIG. 61A

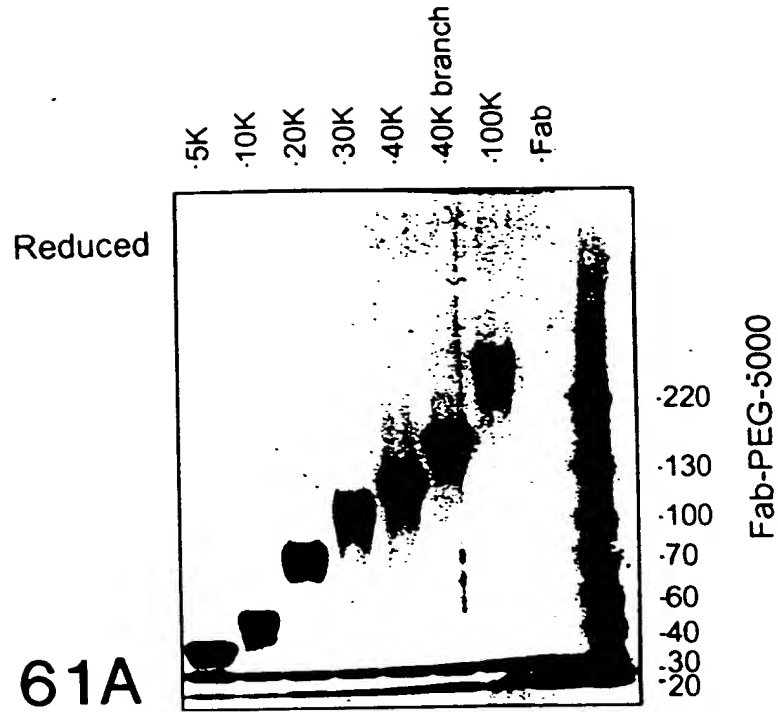
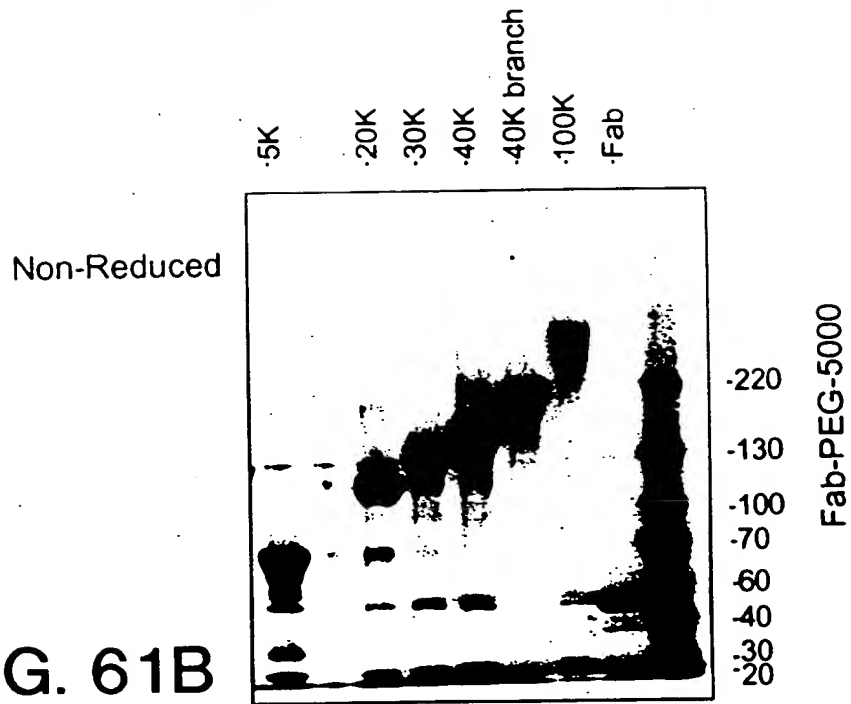


FIG. 61B



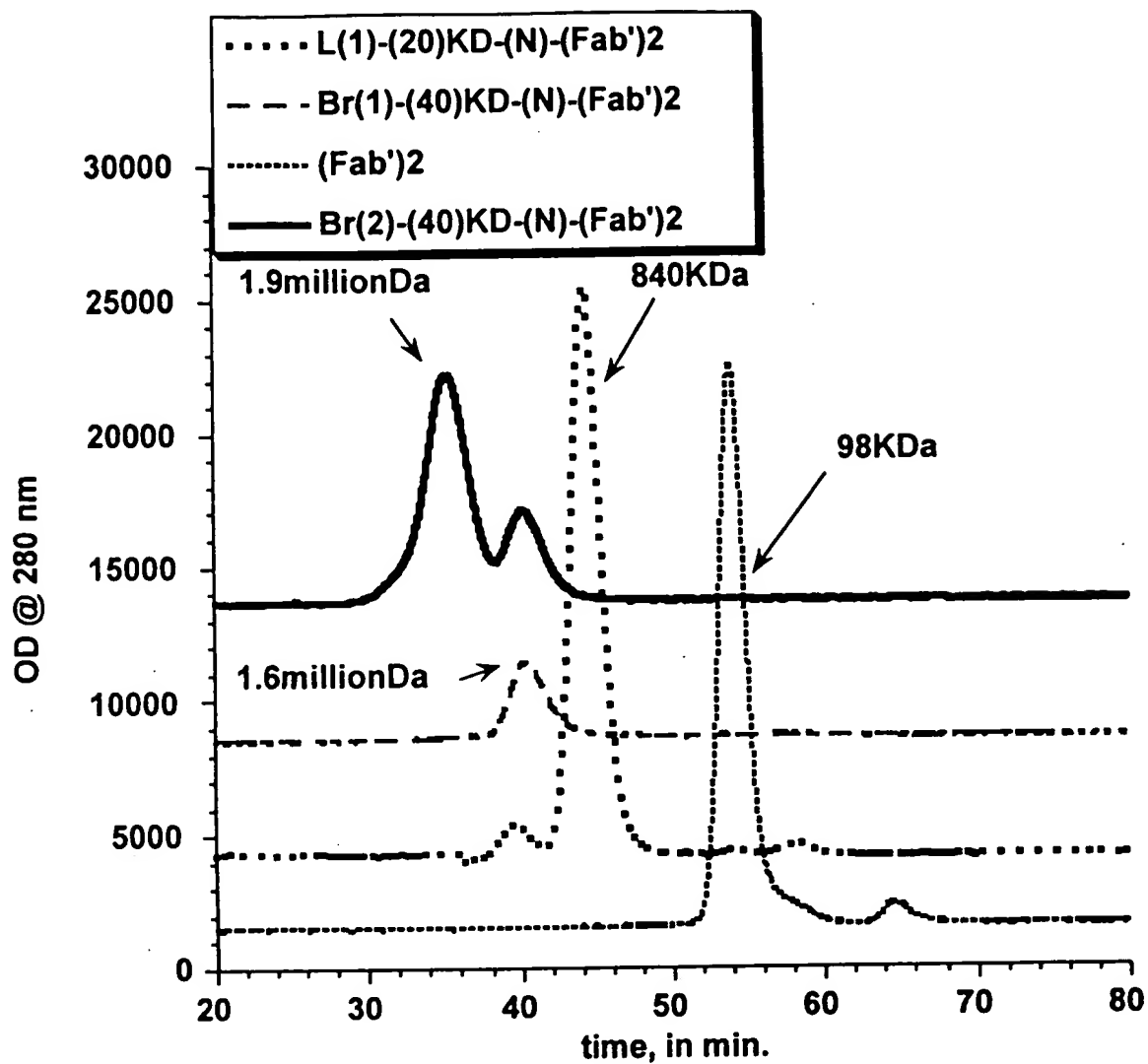


FIG. 62

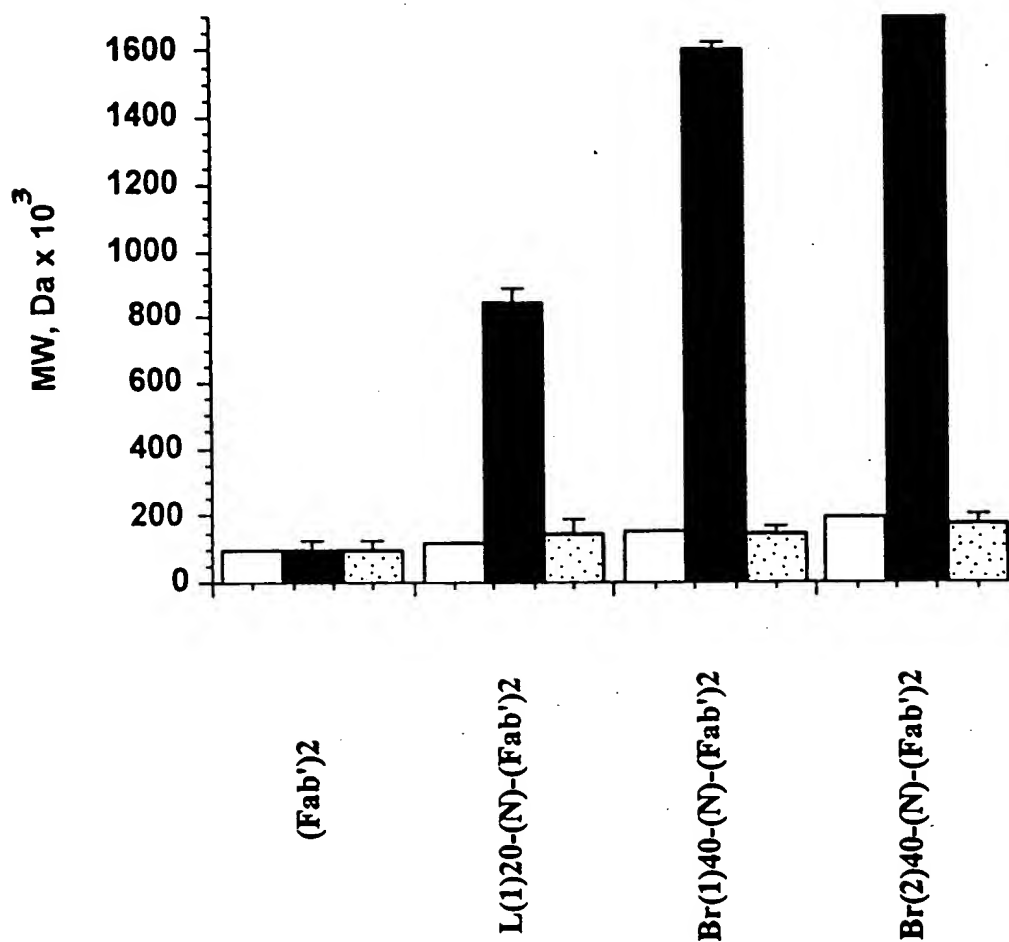
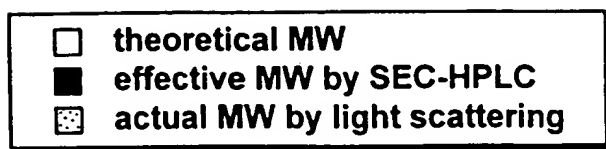


FIG. 63

(Fab')<sub>2</sub>

Br(2) 40kD-(N)-Fab'2

Br(1) 40kD-(N)-Fab'2

L(4+5) 20kD-(N)-Fab'2

L(1)-20kD-(N)-Fab'2

MW markers

kDa

220\_

130\_

90\_

70\_

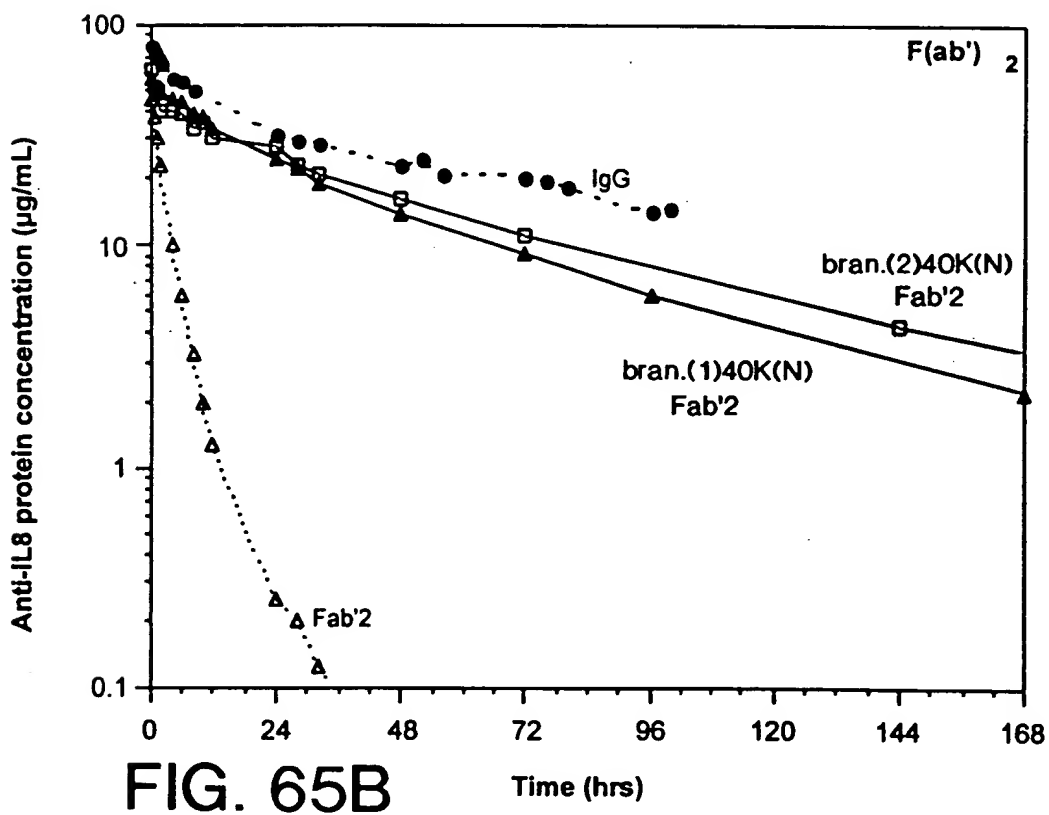
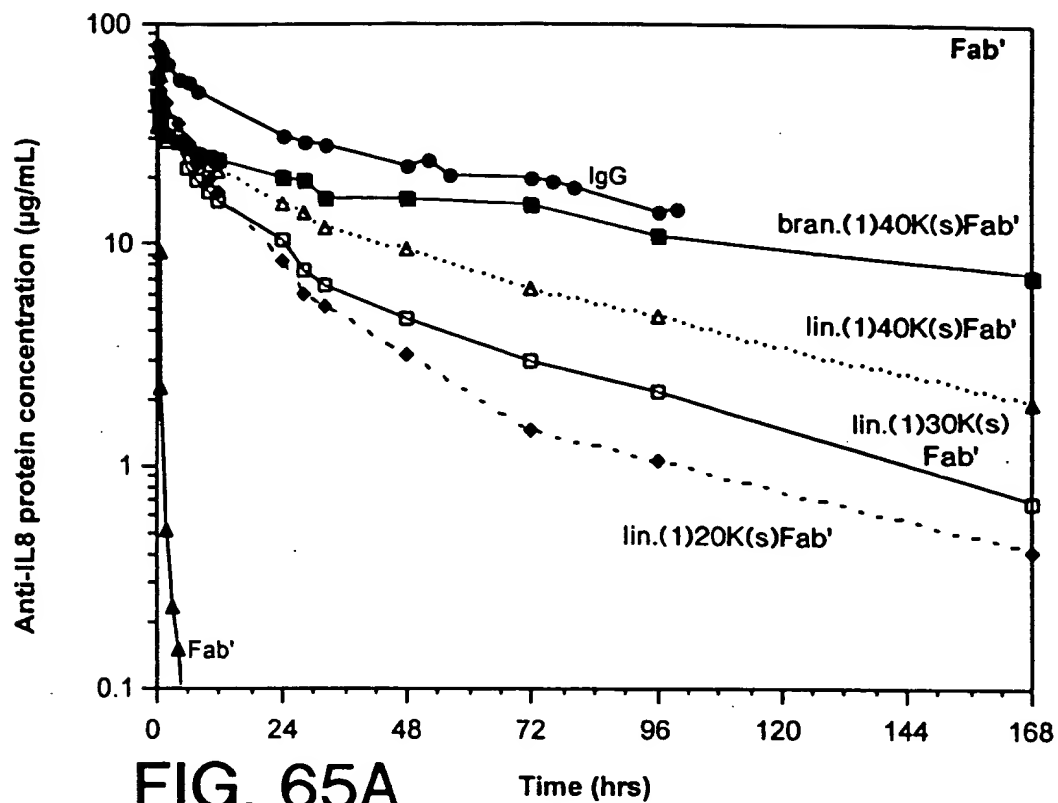
60\_

40\_

30\_

kDa

FIG. 64



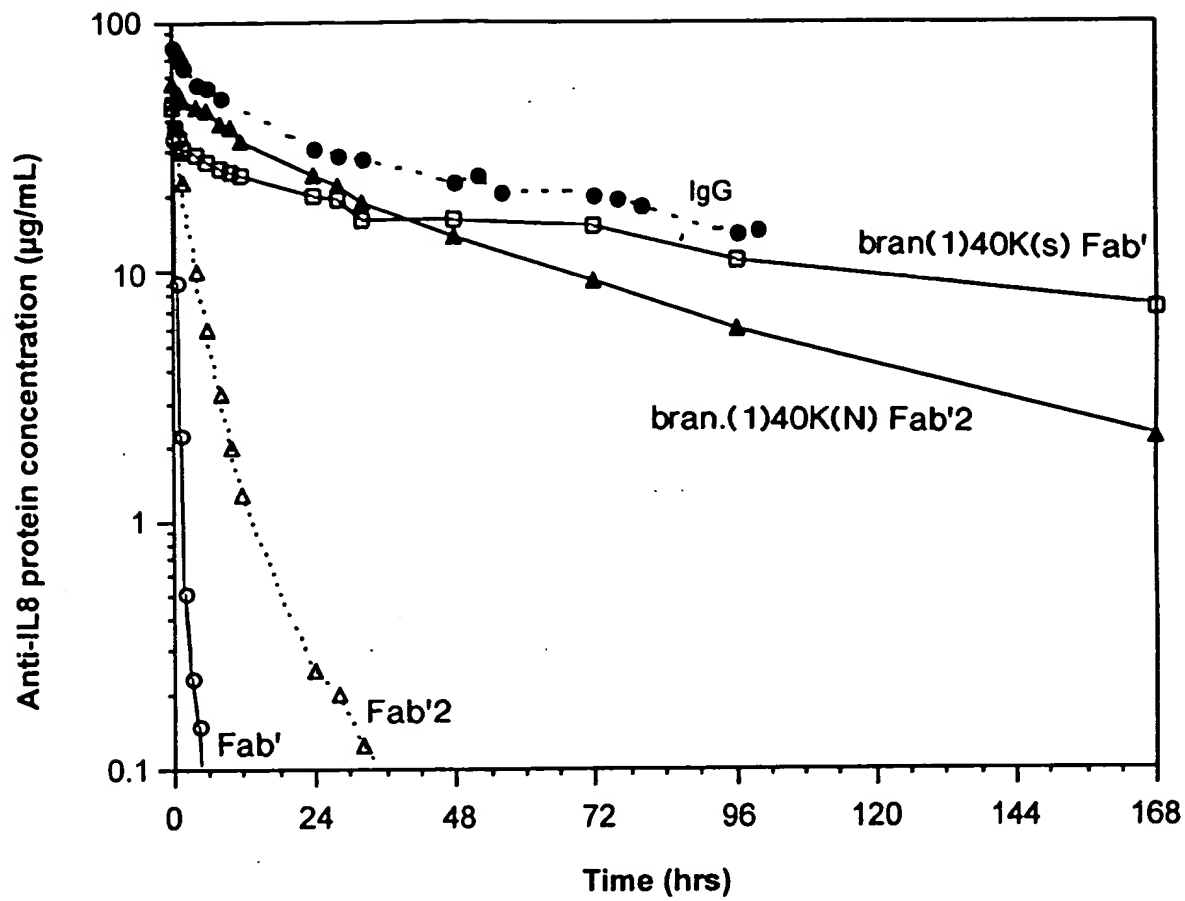


FIG. 66

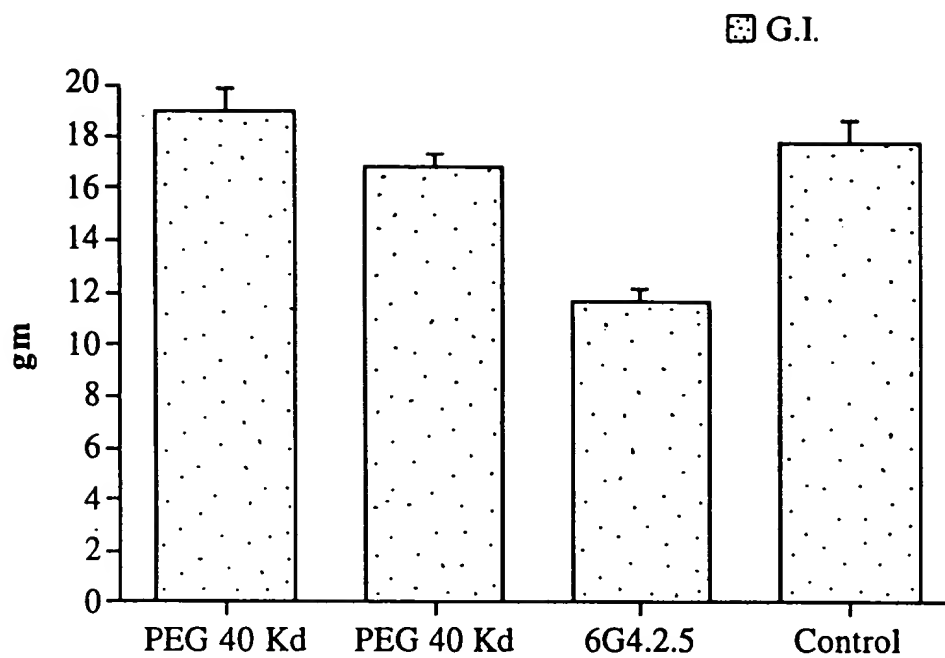


FIG. 67

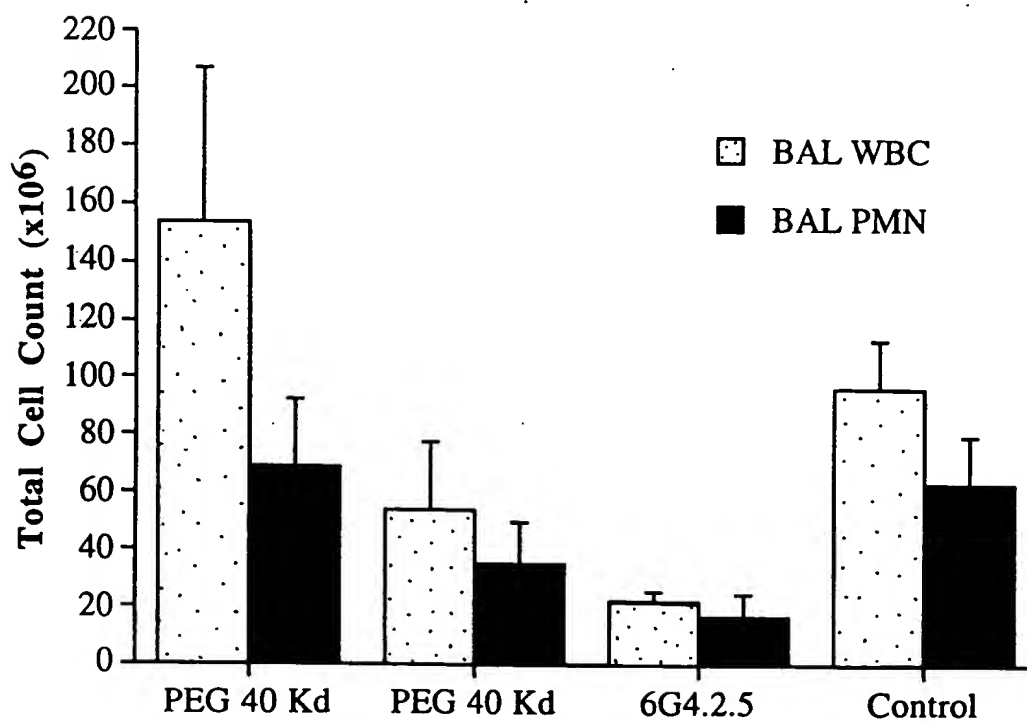


FIG. 68

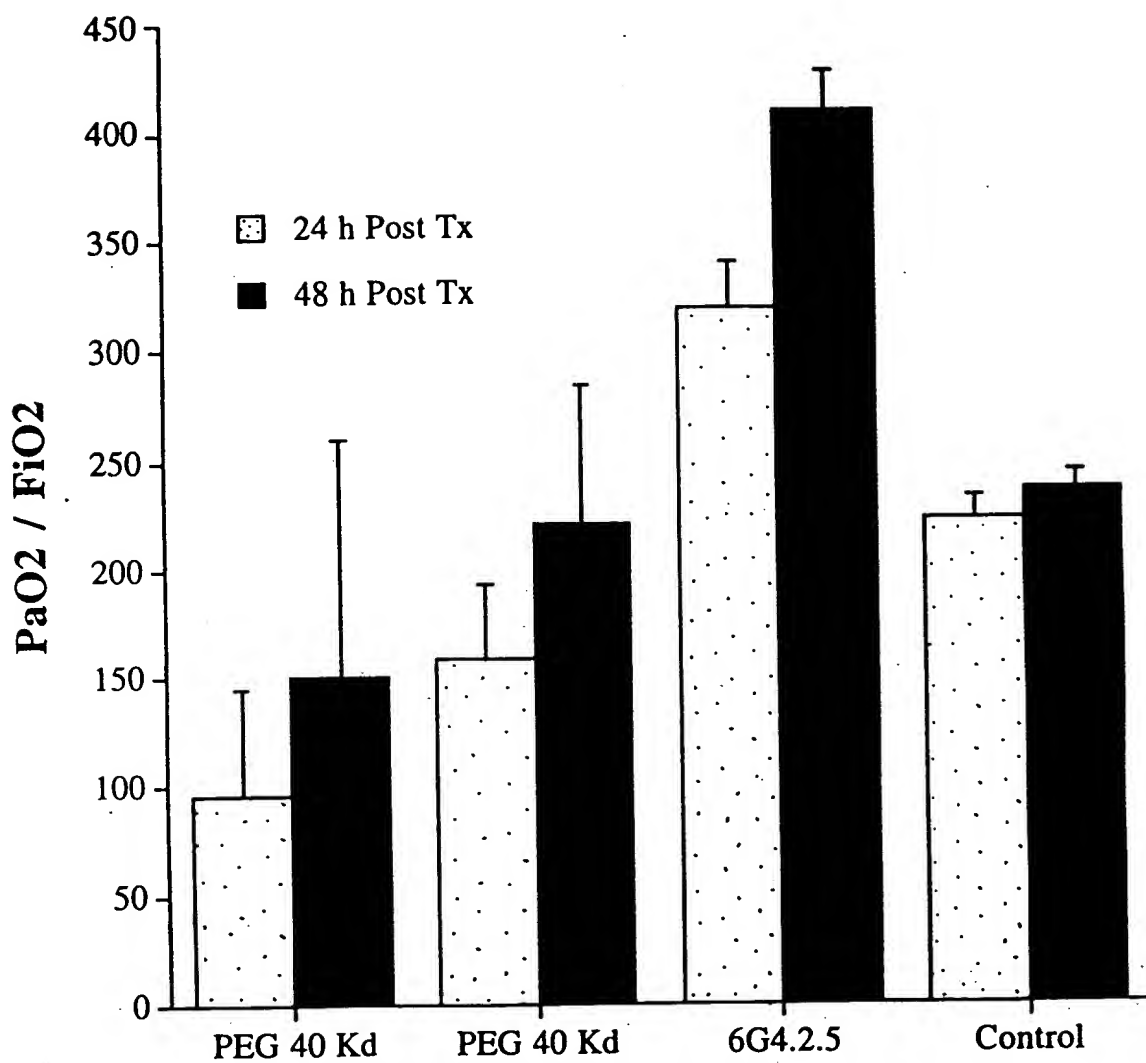


FIG. 69



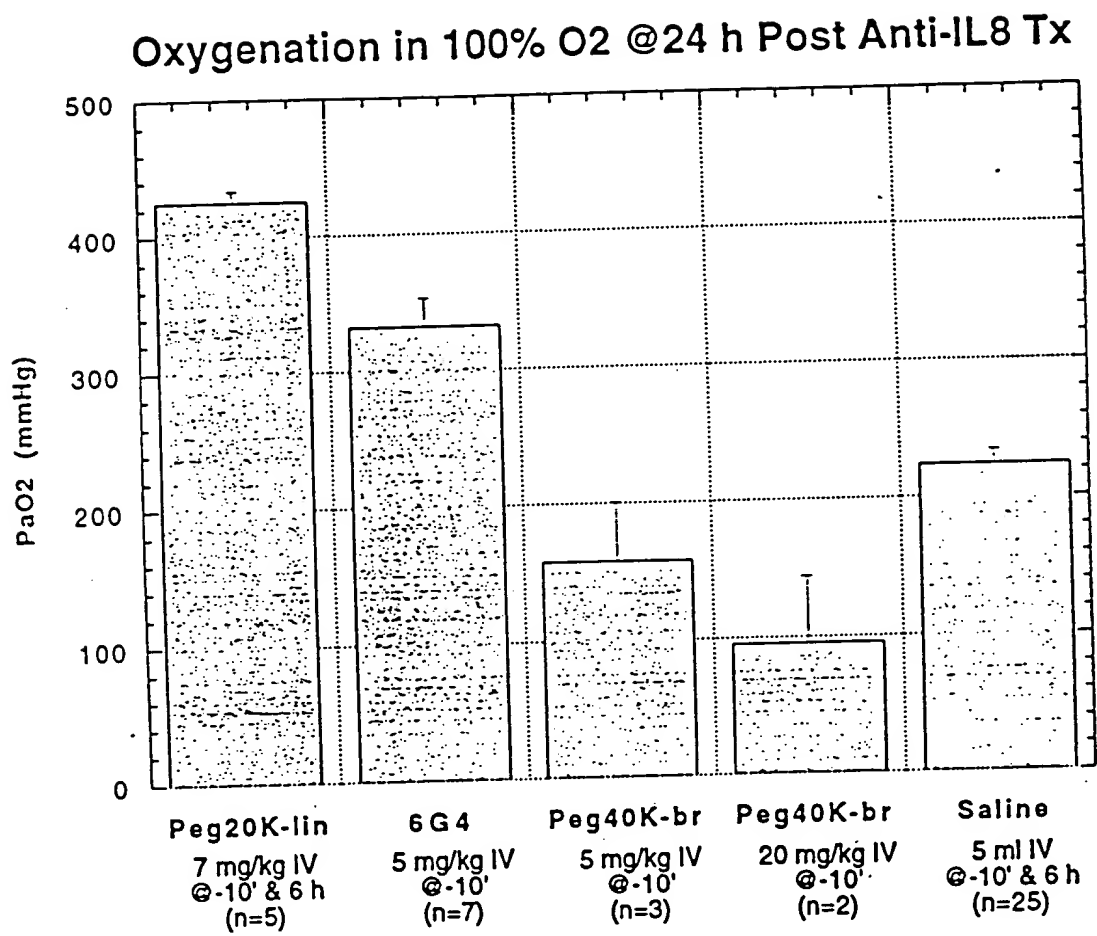


FIG. 70A

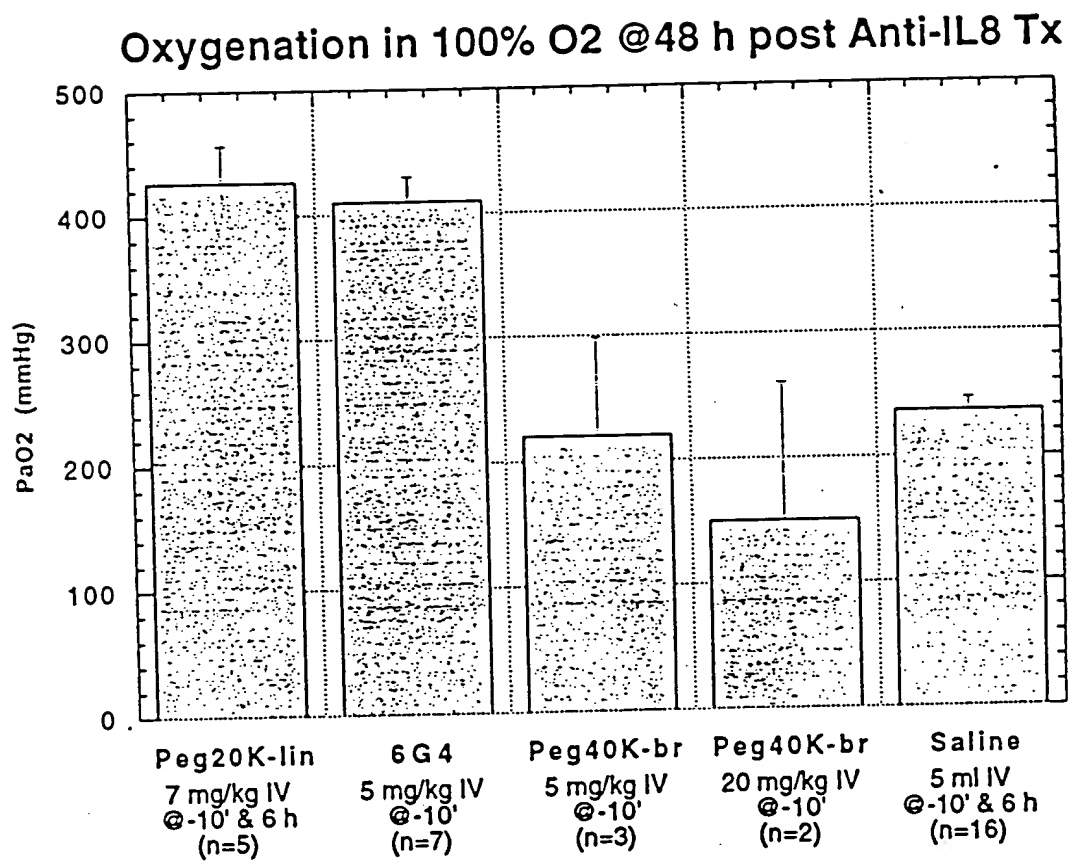


FIG. 70B

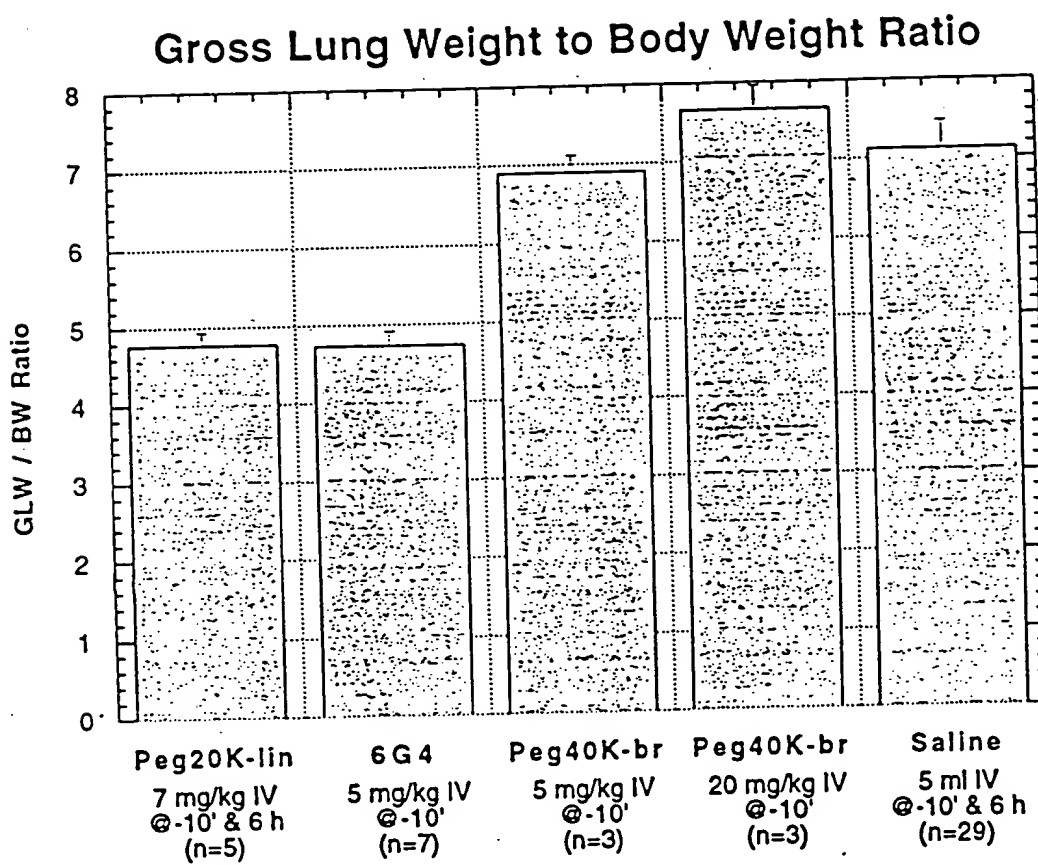


FIG. 70C

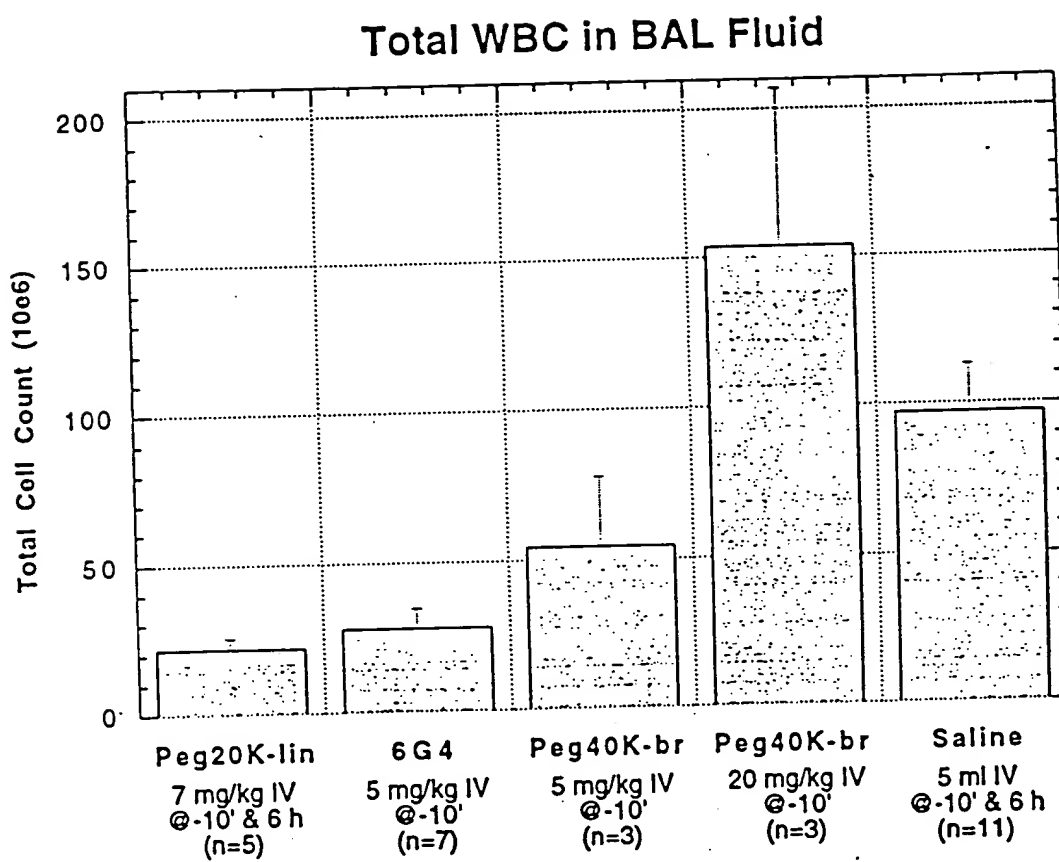


FIG. 70D

### Total PMN in BAL Fluid

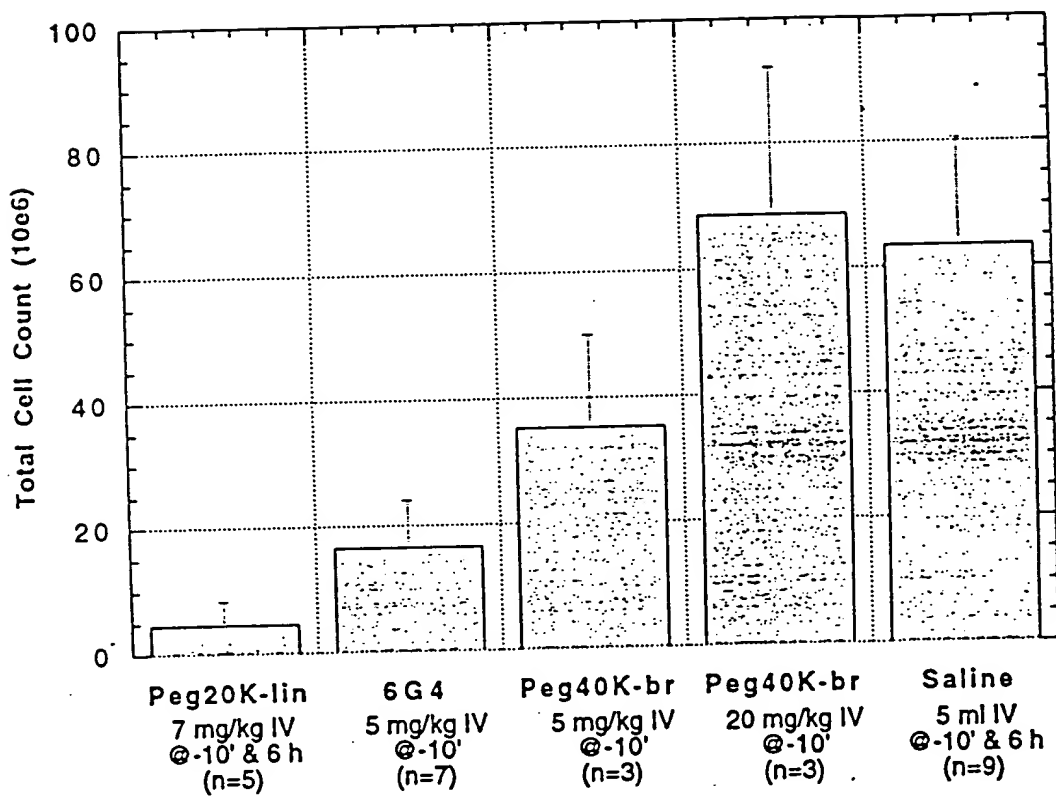
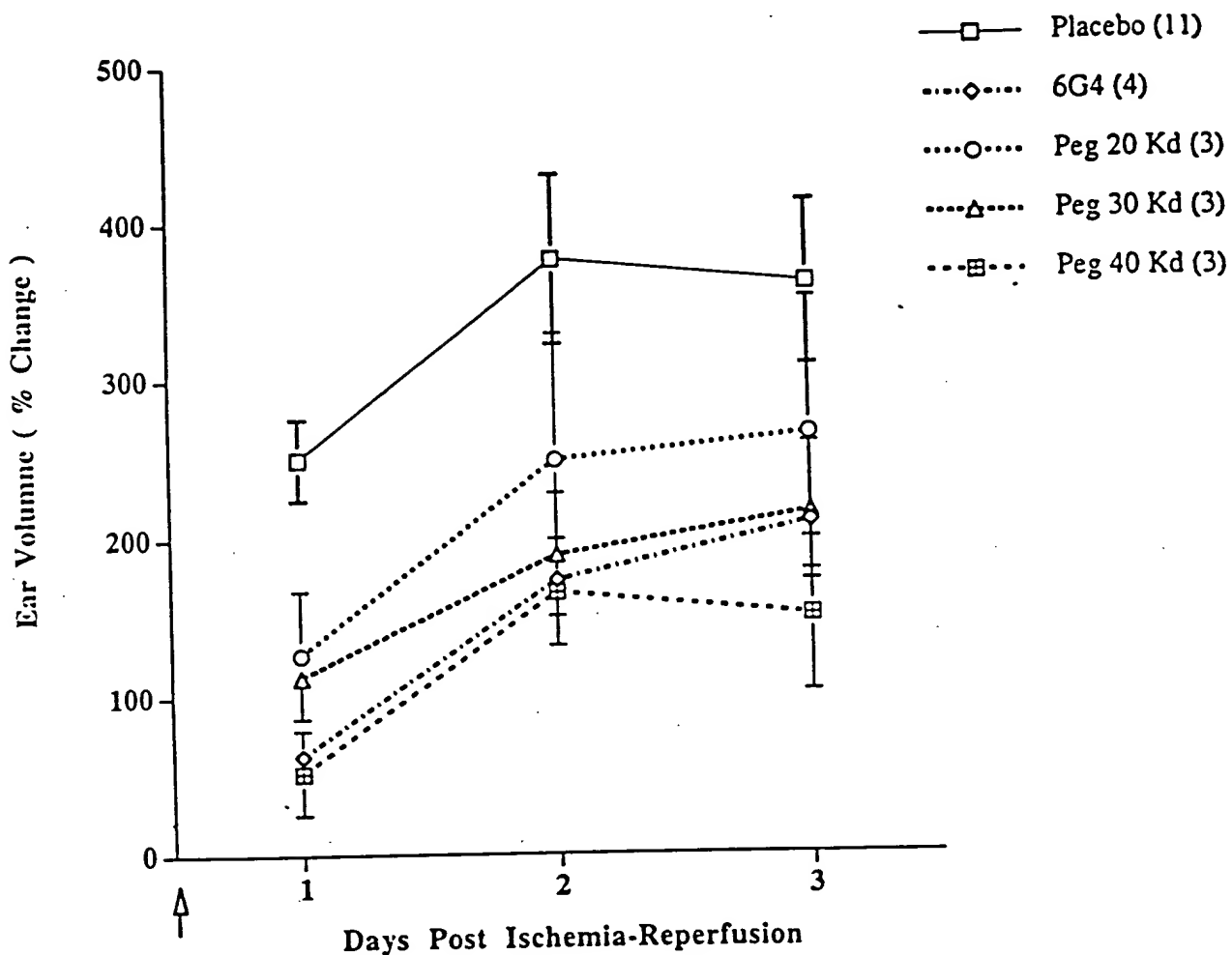


FIG. 70E

## The Effect of Pegylated Anti-IL-8 in the Rabbit Ear model of Ischemia-Reperfusion Injury



Anti-IL-8 formulations :  
Single Dose (5 mg/kg)  
administered IV at time  
of reperfusion

FIG. 71

Figure 72: 20K and 40K PEG rhuMab VEGF Fab (approximately 3 mg/kg  
Serum concentrations following IV administration

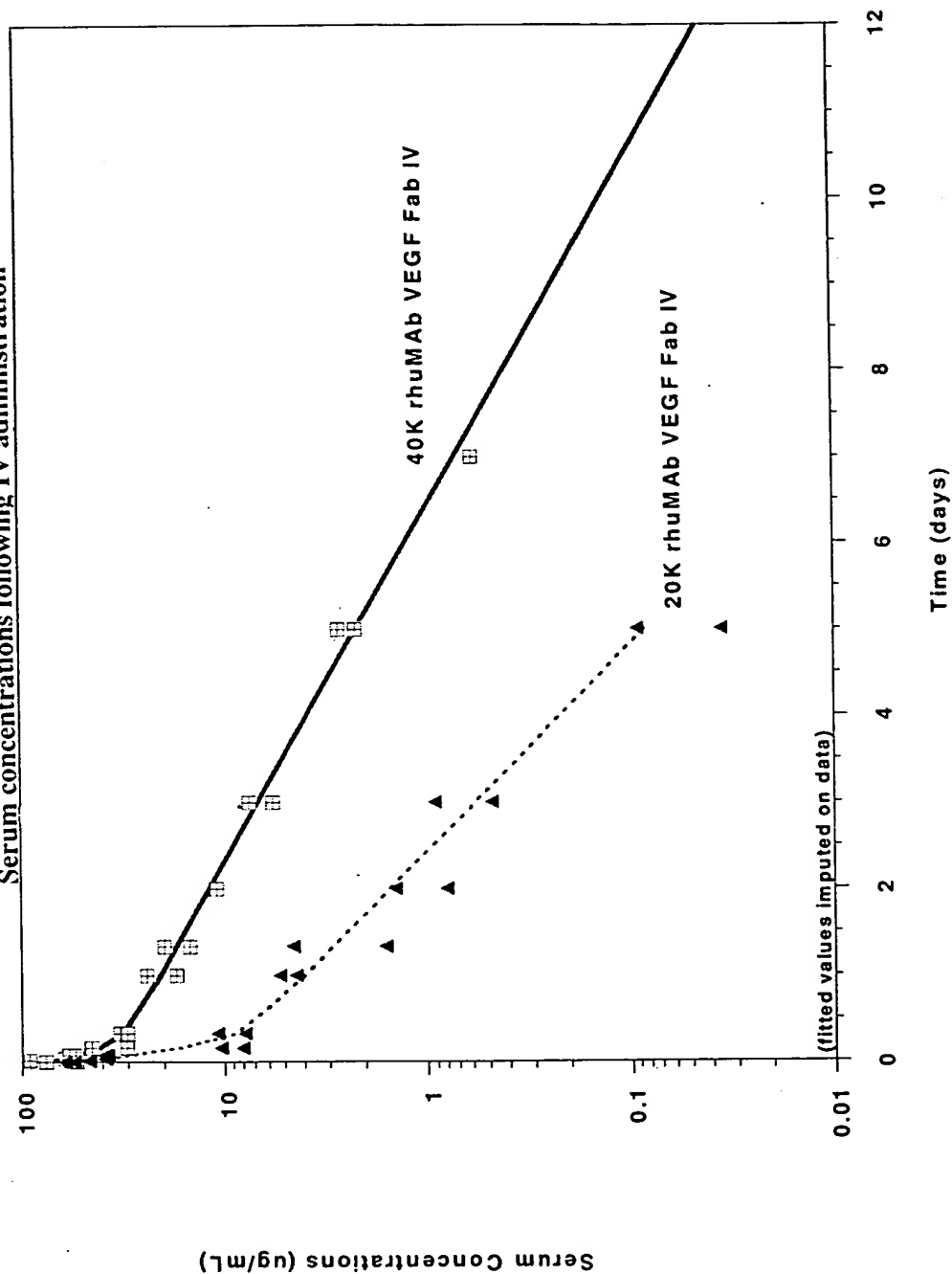
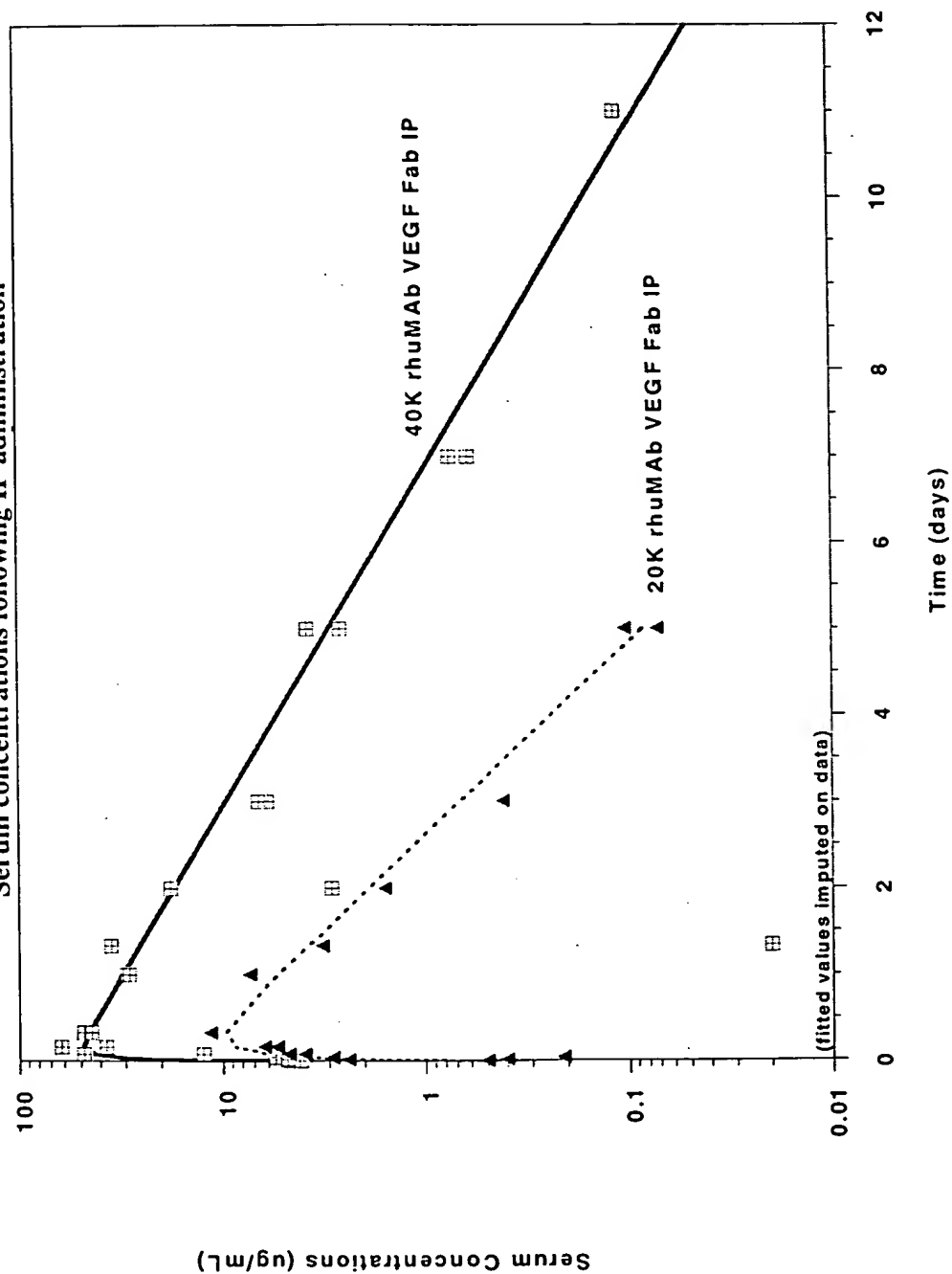


Figure 73: 20K and 40K PEG rhuMab VEGF Fab (approximately 3 mg/kg)  
Serum concentrations following IP administration





# TUMOR WEIGHTS AT NECROPSY 98-277

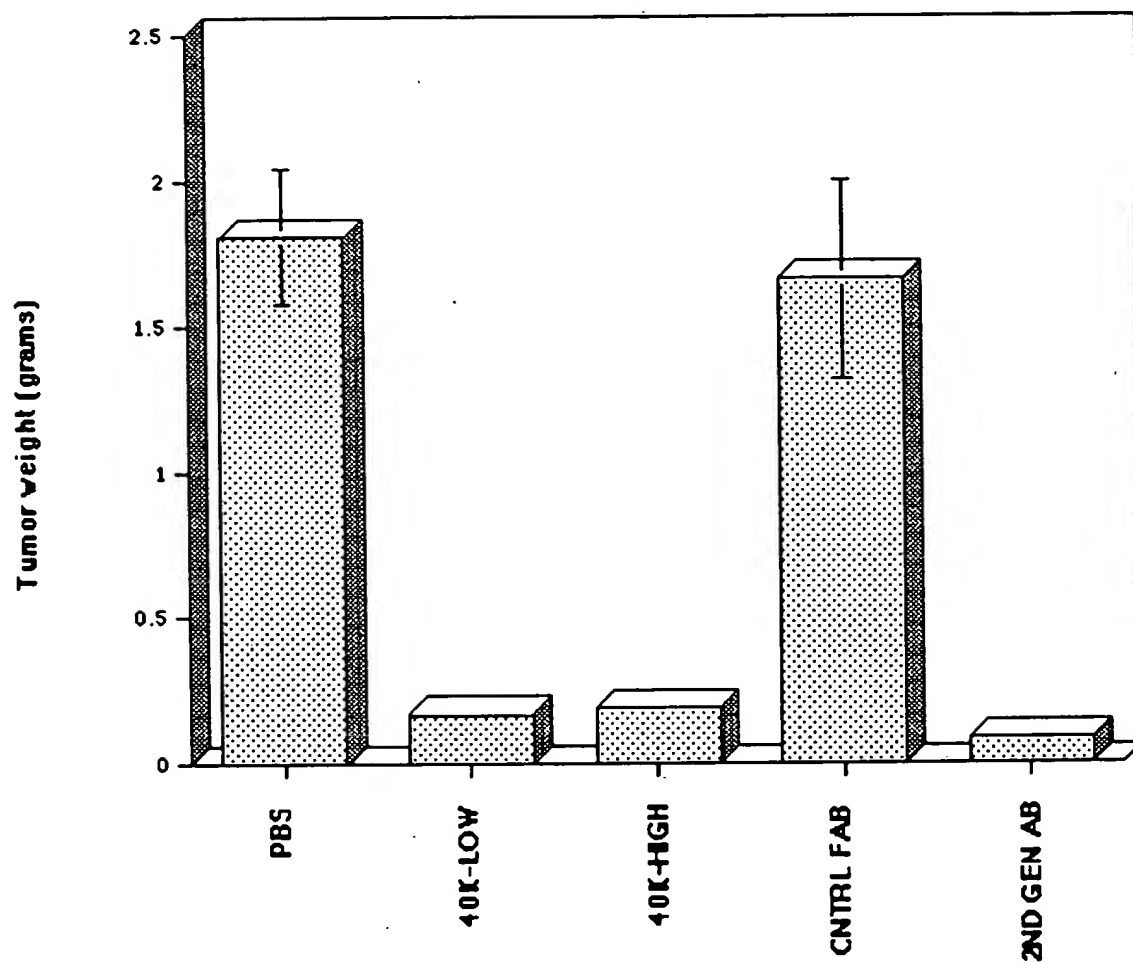


FIG. 74